CARDIOVASCULAR
DISEASE

CARDIOVASCULAR DISEASE

Fundamentals, Differential Diagnosis, Prognosis and Treatment

By

LOUIS H. SIGLER, M.D., F.A.C.P.

Attending Cardiologist and Chief of Cardiac Clinic, Coney Island Hospital; Consulting Cardiologist, Rockaway Beach Hospital; Consulting Cardiologist, Menorah Home and Hospital for the Aged



GRUNE & STRATTON

NEW YORK 1949

GRUNE & STRATTON, INC.
381 Fourth Avenue,
New York 16, N. Y.

PRINTED BY
WAVERLY PRESS, INC
BALTIMORE, U. S. A.
BOUND BY MOORE & CO , INC., BALTIMORE
IN PYROXYLIN-IMPREGNATED WATER-REPELLENT CLOTH

To the Memory of My Mother

Preface

In the employment of the pure sciences in engineering, a project may be carried out with mathematical and mechanical precision and prediction This is not so in the practice of medicine. Here, we can not apply mathematical formulae with exactness. We encounter a great many unpredictable variables and imponderables. This is due to the fact that we are dealing here with the mysterious and unfathomable force known as life This force penetrates every one of the many millions of cells that compose the human organism and it often refuses to conform to our rule.

Largely because of this force with its marked variability in different individuals, the clinician must not only acquire a knowledge of the basic sciences to understand some of the processes taking place in health and disease, but he must also develop the art of the detection of such processes and their correlation Disease must be looked at as a unit affecting the entire organism, even though limited clinically to localized structures or organs, and treatment must be directed to the individual as a whole, not only to the local structures or organs. This is repeatedly stressed and demonstrated in your present text.

Inasmuch as life expresses itself in certain forms of normal and abnormal *physiologic processes, these must be clearly understood to appreciate the* behavior of any individual in health and disease Unfortunately, experimentation in physiology is for the most part carried on by men not directly connected with the practice of medicine Their observations and reports are often submitted in the forms of mathematical formulae and in jargons not entirely or clearly comprehensible to the clinician, even if he wishes to devote his time to their study. The result is that the clinician generally is not sufficiently informed on this most important fundamental branch of the medical sciences

Realizing the need for a proper understanding of the physiologic phe*nomena, as related to clinical medicine, the author of this text devotes con*siderable space to such studies He does it by a simplification of the various observations reported from different sources and by the elimination of confusing detail The essential facts are clearly developed.

In the selection of the numerous references from the literature he attempts to present those which cover the average findings of competent observers. Those controversial factors which are not in general agreement by different observers are discussed from various viewpoints and an attempt is made to reach a decision by deductive reasoning, and based on the personal experiences of the author.

In addition to the physiologic aspects, considerable attention is devoted to the etiology, anatomic pathology and pathogenesis of disease. The psychosomatic aspects of disease are stressed throughout the text and one chapter is fully devoted to it The clinical manifestations of the various diseased states of the circulatory system, the diagnosis and the differential diagnosis are fully covered in a clear, comprehensive manner. The last includes not only the differentiation of the various forms of cardiovascular disease from one another, but also the differentiation of such disease from other diseased states of the body. The prognosis is discussed in each instance from a viewpoint of the clinical manifestations in the given case.

Therapy is considered from a broad constitutional viewpoint, describing the latest measures in considerable detail Proper advice is offered as to the methods to be pursued This is based upon a personal experience of many thousands of cases of cardiovascular disease followed by the author in an extensive hospital and consultation practice of over twenty-five years.

The text attempts to cover all problems the physician is called upon to solve in the course of his practice, as submitted to the author in his capacity as consultant. These are presented in a simple and an easily comprehensible form The method of presentation is the one used by the author in postgraduate teaching for many years.

The newer methods employed in diagnosis, such as roentgenkymography, electrokymography, angiocardiography and cardiac catheterization are briefly discussed Although these methods are limited to a few who have developed the technics and have experience in their proper performance, they are discussed here in order to inform the clinician of their significance and value. The same is true of the older diagnostic methods employed, such as phonocardiography and pulse recording, which are briefly described

The text is divided into thirty-one chapters. The first deals with the general incidence of cardiovascular disease to point out the enormity of the problem. The second deals with the etiologic factors of disease generally, which affects also the cardiovascular system The third and fourth chapters deal, respectively, with much-needed reviews of the normal anatomy and physiology of the cardiovascular system—subjects which are usually forgotten by the average physician who has been out of college for any length of time, and which are essential for a proper understanding of disease processes Chapters five to eleven deal with the normal objective findings of the cardiovascular system and the various abnormalities encountered in disease. Chapters twelve to fifteen describe the various subjective expressions of cardiovascular disease Chapter sixteen deals with the manifestations of shock and Chapters seventeen to thirty-one with the various specific conditions or pathologic states affecting the cardiovascular system.

The subject matter is fully illustrated by clinical material, roentgenologic

findings, pathologic specimens including photomicrographic studies and many original drawings and illustrations.

As the book is purely a text on the clinical aspects of cardiovascular disease, the value of the electrocardiogram is merely pointed out from time to time in the diagnosis of the various conditions A full description of the electrocardiographic findings in the various diseased states as well as electrocardiographic interpretations are given in the author's previous text, "The Electrocardiogram: Its Interpretation and Clinical Application," first published in 1944.

The author wishes to express his thanks to Dr. Harold Fink, pathologist of the Coney Island Hospital, Brooklyn, who very kindly supplied and discussed some of the pathologic specimens. He also wishes to express his thanks to Dr Silik H. Polayes, pathologist of the Cumberland and Prospect Heights Hospitals, Brooklyn, for several of the pathologic specimens he supplied and for the help he gave in their preparation. Some of the pathologic specimens of congenital heart disease were supplied by Dr. Jesse E. Edwards of the Mayo Clinic; those of the muscular layers of the heart by Dr Jane S Robb of Syracuse Univeristy, and those of the injected coronary vessels, by Dr. Monroe J. Schlesinger, of the Beth Israel Hospital, Boston To each of them, the author wishes to express his appreciation

He also wishes to express his affection and thanks to his devoted wife, their daughter June and son Stephen, whose encouragement, careful review and criticism of the manuscript helped perfect this volume Until they finished reading the manuscript, the author did not realize how many commas, colons and semicolons he sacrificed, and how many dangling participles he used.

His secretary, Miss Edith Hamburg, has done a splendid job in typing the manuscript. Mrs Cele Ticktin splendidly executed the original drawings and the rest of the Bergman Associates the photography and photomicrographs. To all of them the author offers his thanks. Finally, he wishes to thank Mr. Henry M Stratton, his publisher, at whose insistence this work was undertaken, and who gave the author every encouragement in its completion.

LOUIS H SIGLER, M D

Brooklyn, N Y.
April 1949

Contents

CHAPTER I
General Incidence of Cardiovascular Disease

BEFORE commencing the study of cardiovascular disease, it is of interest to have some idea of its incidence. This may be obtained from an analysis of the mortality tables of the United States Vital Statistics, Special Reports.[1, 2, 3] Although these tables cover only the *mortality* incidence and not the *morbidity*, a rough estimate of the latter may be made from the number of deaths as well as from other sources to be described later.

Inasmuch as the sources of the vital statistics are widely varied, being derived from different parts of the country, and are dependent upon the certifications by different physicians using varying criteria, the specific diagnoses in many instances may not be entirely reliable. Nevertheless, since we are interested, in this chapter, in the general incidence of cardiovascular disease, not in specific types, the vital statistics reports are ample for the purpose. They give us an excellent bird's eye view of its prevalence.

Total Deaths from Cardiovascular Disease. According to the figures obtained from the various tables, cardiovascular disease is the leading cause of death in this country as well as in many other parts of the world. If we take the year 1944 as an example, the number of deaths in the United States from all causes in that year was 1,411,338. Of these deaths, 418,062 or about 29.6 per cent were due to various forms of heart disease. In addition, there were 32,501 deaths from general vascular disease such as aneurysms, general arteriosclerosis, gangrene, high blood pressure and so on and 124,250 deaths from intracraneal lesions of vascular origin, making a total of 156,751 or about 11.1 per cent of deaths due to all vascular disease. These make a total of 607,314 deaths attributable to cardiovascular disease, comprising nearly 41 per cent of all deaths. In addition, there were 1,471 deaths due to rheumatic fever, 34,948 to diabetes, 2,660 to exophthalmic goiter and 91,687 to nephritis, making a total of an additional 130,766 or about 9.3 per cent where cardiovascular complications are frequently present and were perhaps partly responsible for death. The grand total, then, of deaths directly attributable to heart disease or with possible cardiovascular involvement, would thus be 705,579 or about 50 per cent of all deaths. These are expressed in Table 1 and Figure 1.

Death Rate from Heart Disease Compared with Other Leading Causes: The importance of heart disease in itself as a cause of death, exclusive of vascular disease, is illustrated in Table 2 and Figure 2, showing the death rates from heart disease and various other leading causes in 1944 per 100,000

estimated population. It will be seen that heart disease is first on the list, with a great preponderance in death rate over any other cause. Its rate in the United States was 315 4 per 100,000 population compared with that of its next competitor, cancer, which contributed a death rate of 129.1 per 100,000.

Death Rate in Relation to Race and Sex: It will be observed in the same Table and Figure that heart disease contributes more to the death rate in

TABLE 1 —*The Relation of Deaths Due to Cardiovascular Disease and Disease with a Possible Cardiovascular Element to the Total Deaths United States, 1944*

Cause of death	*Number of cases*	*Rate per 100,000 estimated population*	*Percentage of total deaths*
All causes	1,411,338	1,064 7	
Heart disease	418,062	315 4	29 6
Intracranial lesions of vascular origin	124,250	93 7	8 8
Other vascular disease	32,501	24 5	2 3
Total cardiovascular disease	574,813	433 6	40 7
Disease with possible cardiovascular element	130,766	98 7	9 3

TABLE 2 —*Death Rates per 100,000 Population, Excluding Armed Forces Overseas, for Nine Leading Causes of Death, by Race and Sex United States, 1944*

Cause of death	*All races, both sexes*	*White*		*Nonwhite*	
		Male	*Female*	*Male*	*Female*
All Causes	1,064 7	1,225 7	876 7	1,392 0	1,109 9
Diseases of the heart	315 4	398 6	254 2	274 3	220 6
Cancer and other malignant tumors	129 1	135 5	133 3	75 6	92 2
Intracranial lesions of vascular origin	93 7	93 8	90 0	107 0	113 4
Accidents (all forms)	71 8	105 2	41 3	108 3	36 8
Nephritis	69 2	72 4	57 9	115 5	97 7
Pneumonia (all forms), influenza	61 7	67 1	47 1	122 1	88 4
Tuberculosis (all forms)	41 3	45 0	23 3	122 7	91 3
Diabetes mellitus	26 4	21 1	32 9	13 2	24 7
Premature birth	25 0	28 1	19 3	41 8	33 6

the white race than in nonwhites. In both races it is much greater in the male than in the female sex Intracraneal lesions of vascular origin, on the other hand, occur more frequently among the nonwhites than whites

✓*Death Rate in Relation to Age* Although death from heart disease and intracraneal lesions of vascular origin occurs at all ages, its greatest incidence begins at about 40 years of age and progressively increases to about 80 years when it begins to fall again. This is illustrated in Table 3 and

Figure 3. The reason for the rise in the death rate from these causes after 40 years is that arteriosclerosis is the main etiology of heart disease and intracraneal lesions of vascular origin after that age, and due to the progressive increase in the frequency of arteriosclerosis after 40 years of age, the incidence of cardiac and cerebral vascular disease correspondingly increases. After 80 years, on the other hand, the population remaining alive is small and diminishes progressively as age advances. Hence, although the predominance of death after 80 is due to the effect of arteriosclerosis, the actual number of deaths is naturally comparatively small.

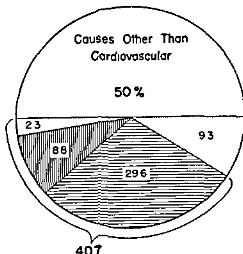


Fig 1—Percentage of Deaths due to Actual and Potential Cardiovascular Disease Compared with that due to All Other Causes, United States, 1944 Section with horizontal lines, percentage of deaths due to heart disease; dark vertical lines, various forms of vascular origin, light vertical lines, intracranial lesions of vascular origin, dotted section, rheumatic fever, diabetes, hyperthyroidism and nephritis with potential cardiovascular disease, light section, other than cardiovascular causes.

Recent Increase in Mortality from Heart Disease: The mortality from heart disease has shown a progressive increase in the United States since 1900, when accurate vital statistics recordings were started. This is demonstrated in Table 4 and Figure 4, showing the mortality incidence and rate from heart disease in the given years between 1900 and 1940. For the years 1918 to 1922, the incidence and rate are presented for each year to illustrate the possible effect of the 1918 influenza epidemic on the cardiac mortality figures.

Possible Causes of the Increase in Mortality: The causes of the recent increase in mortality may be many. One of them may be the marked in-

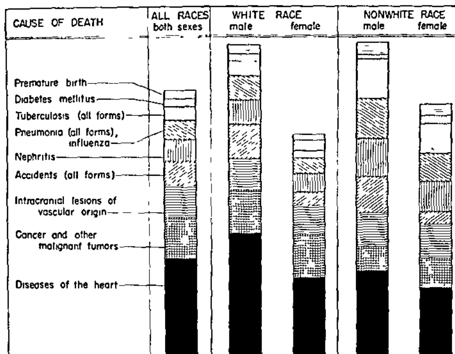


FIG 2 —A COMPARISON OF THE DEATH RATES FROM HEART DISEASE AND OTHER LEADING CAUSES, IN THE WHITE AND NONWHITE RACES, MALES AND FEMALES, UNITED STATES, 1944 For figures, see table 2

TABLE 3 —*Deaths from Heart Disease and Intracranial Lesions of Vascular Origin at Various Ages United States, 1944*

Ages in Years	*Number of Deaths* Heart disease	Intracranial lesion of vascular origin
Total all ages	418,062	124,250
Under 1	181	172
1–9	835	245
10–19	2,051	251
20–29	3,648	668
30–39	9,890	1,994
40–49	29,217	7,121
50–59	66,418	17,611
60–69	103,633	30,858
70–79	121,264	39,881
80–89	70,611	22,632
90–99	9,711	2,637
100 and over	328	79
Not stated	275	101

crease in the population in the United States over this period. However, this would account for only a small part of the increase in deaths from

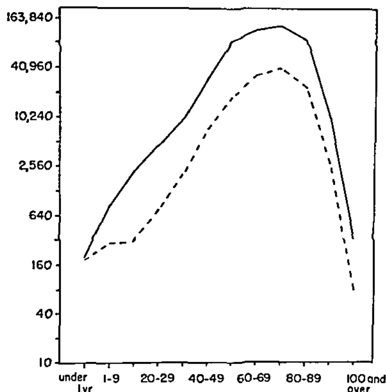


FIG 3—NUMBER OF DEATHS FROM HEART DISEASE AND INTRACRANEAL LESIONS OF VASCULAR ORIGIN AT VARIOUS AGES, UNITED STATES, 1944 Solid curve for heart disease Broken curve for intracraneal lesions of vascular origin

TABLE 4—*Mortality Incidence and Rate from Heart Disease between 1900 and 1944, Abbreviated from the Mortality Summary for U S Registration States*

Year	*Number of deaths*	*Rate per 100,000 estimated population*
1900	27,427	137 4
1905	35,252	161 9
1910	75,429	158 9
1915	101,429	163 9
1918	135,585	171 06
1919	123,007	147 9
1920	137,374	159 6
1921	137,157	156 2
1922	152,968	165 0
1925	188,554	184 8
1930	251,153	214 2
1935	312,333	245 4
1940	385,191	292 5
1944	418,062	315 4

heart disease inasmuch as not only the number of deaths but also the death rate per 100,000 estimated population during each period shows a progressive upswing If the death increase was due only to an increase in the population, the death rate per 100,000 estimated population at each interval would remain about the same. This leaves no doubt that the increase in the incidence of heart disease over these years is largely caused by additional factors. Increased general longevity must be regarded as outstanding among these, and although it naturally results in population increase, it must be considered apart from such mechanical causes as birth rate changes, emigration, etc.

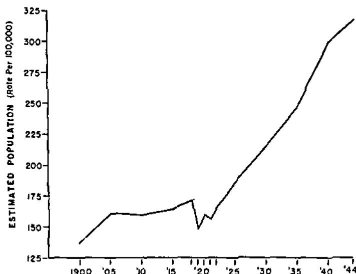
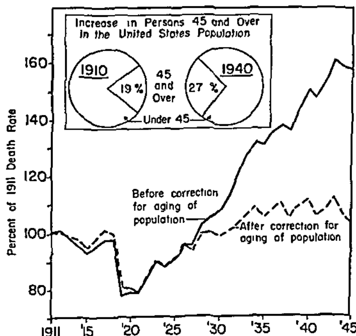


FIG 4—MORTALITY RATE FROM HEART DISEASE PER 100,000 POPULATION, IN THE GIVEN YEARS, 1900 TO 1944, UNITED STATES There is a progressive rise in death rate over these years, except for the drop between 1919 and 1922, due undoubtedly to the 1918 influenza epidemic See text and table 4

One of the most important factors in today's increased longevity is a marked decrease in infant and child mortality in the past 40 years, due to tremendous strides made in preventive medicine A greater part of the population carried off in previous years by acute infectious and contagious diseases reaches the arteriosclerotic age and dies from cardiovascular disease. The recent introduction of chemotherapeutic and antibiotic measures in the treatment of infections and infectious diseases further increased the general longevity. Inasmuch as the figures in Table 4 are the crude deaths from heart disease, they do not take into consideration the increase in the general span of life. Figure 5 illustrates the percentage increase in

the United States population in persons over 45 years in 1940 as compared with 1910 and the effect of aging of the population on the mortality rate from heart disease.

An interesting illustration of the possible effect of an epidemic of infectious disease on the change in the incidence and rate of deaths from heart disease is shown in the mortality figures during the years 1918 to 1922, compared with the other years, as illustrated in Table 4 and Figure 4. In 1918 the rise in the death incidence and rate was approximately that ex-



Industrial Policyholders,

levels The rate per 100,000 of the population, however, remained smaller than in 1918. These figures may be explained only on the basis of the

The great general improvement in hygienic conditions and the elimination of much of the infections and infectious diseases are partly responsible not only for the increase in longevity and therefore in the increase in the total incidence of cardiac disease but also for an increase in other diseases of advancing years such as cancer. A definite change in the position of the various diseases in the mortality tables is seen when we compare the relative frequency of the causes of death in 1900 and each subsequent decade to 1940 and later For example, in 1900, tuberculosis was the leading cause of death in the United States with a mortality rate of 195 per 100,000 population In 1946, the total number of deaths from this disease was about 50,000 with a rate of only 36 per 100,000 During this period of over 40 years, tuberculosis thus sank from a first rank killer to a seventh rank. If the 1900 rate would still prevail in 1946, the number of deaths from this

TABLE 5 —*United States Death Rates from Heart Disease per 100,000 Estimated Population in the Various Age Groups in the Given Years*

Ages	Years				
	1900	*1910*	*1920*	*1930*	*1940*
All ages	137 4	158 9	159 6	214 2	292 5
Under 1 year	147 8	99 2	52 0	33 1	17 5
1–4 years	15 0	12 8	9 7	6 9	3 6
5–14 years	23 3	22 3	17 4	12 1	8 0
15–24 years	28 8	26 7	24 5	21 3	14 0
25–34 years	43 4	40 8	37 5	38 2	29 7
35–44 years	80 8	85 7	73 1	89 4	91 7
45–54 years	173 0	189 5	171 6	238 9	279 5
55–64 years	414 1	480 7	452 0	598 6	713 5
65–74 years	957 3	1,191 7	1,200 9	1,493 9	1,723 5
75 years or over	1,819 7	2,667 6	3,186 8	3,931 9	4,813 2

disease in 1946 would have been 273,000 instead of 50,000, because of the great increase in population

The shift of the mortality incidence of disease from the younger to the more advanced age groups caused a change also in the mortality rates from heart disease itself in the various age groups. The death rate from heart disease in early life, which is predominantly of the rheumatic form, has progressively diminished since 1900. On the other hand, the death rate from heart disease in later life, which is predominantly of the arteriosclerotic form has progressively increased over the same period of time. This is clearly illustrated in Table 5 and Figure 6, showing the death rates per 100,000 population in the various age groups in the given years. It will be noted that up to 35 years of age the mortality rate from heart disease was greater in 1900 than in 1940, and the diminution for each age group was

progressive in each decade between 1900 to 1940. After 35 years, the reverse is true. The death rate increased with increase in age in the various age groups in 1940 compared with that of 1900, and the increase was in reverse direction.

Geographic Distribution of Heart Disease Although the increase in population and the increase in general longevity are probably mainly responsible for the increase in the death rate from heart disease, there are undoubtedly many additional factors which are partly responsible for such increase One of these may be the improvement in the criteria for diagnosis of cardiovascular disease Other factors may be the increased tempo in our mode of living, overcrowding in some parts of the country, increased mental and

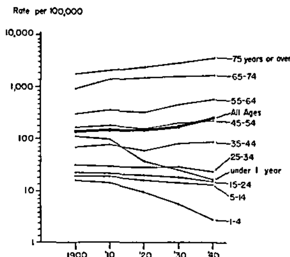


FIG 6 —DEATH RATE PER 100,000 POPULATION IN THE VARIOUS AGE GROUPS IN THE GIVEN YEARS 1900 TO 1940. For significance, see text

physical strain in other parts, climatic conditions, type and variety of food intake and various other causes to be described in the following chapter.

That these various elements may play a part in increasing the incidence from heart disease appears to be evidenced by the fact that the death rate from such disease varies in different parts of the country and the world generally It appears to be greater in those parts where industry and commerce are most highly developed. It also appears to be greater on the average in the overcrowded urban districts than in rural areas where there is more open air life, purer air and a more relaxing environment. These are illustrated in Table 6 and Figure 7 showing the mortality incidence from heart disease in the various geographic subdivisions of the United States in

1940. The comparative death rate in the corresponding urban and rural districts are shown in Figure 8 and also in Table 6.

TABLE 6.—*Death Rates from Heart Disease per 100,000 Estimated Population by Geographic Division and by Urban and Rural Districts: United States, 1940*

Geographic division	Total all ages, races and both sexes	Place of residence: Urban	Place of residence: Rural
United States	292.5	338.7	250.6
New England States	391.0	393.4	387.8
Middle Atlantic States	366.7	362.3	378.5
East North Central States	320.3	323.3	321.5
West North Central States	270.8	321.4	244.6
South Atlantic States	227.1	294.6	190.3
East South Central States	193.3	285.6	167.2
West South Central States	190.5	269.7	158.5
Mountain States	224.6	309.2	188.5
Pacific States	347.4	379.2	300.5

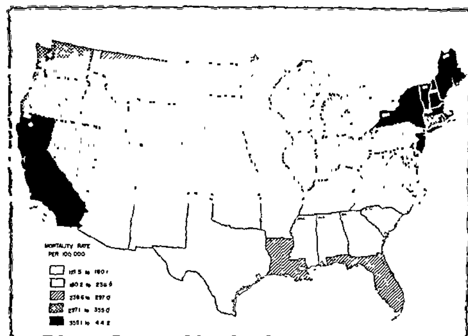


FIG. 7.—MORTALITY RATE FROM HEART DISEASE IN THE VARIOUS STATES, IN 1940

It will be observed that the mortality rates in different parts of the country show marked fluctuations. The highest rate occurred in the New England states where the average mortality was 391.0 per 100,000 of the population and the lowest in the West South Central states with an average

mortality rate of only 190 5 per 100,000 population. The individual states in the various sectional areas show in many cases a fairly uniform death rate, but in others there is a marked fluctuation. For instance, in the South Atlantic states, the death rate in Maryland was 347.9 whereas in North Carolina, it was only 166 8. The greatest fluctuations occurred, however, between states far apart in distant geographic subdivisions. Thus, in New Mexico, the death rate was 121.5, the lowest in the United States, and in New Hampshire, the rate was 414, which is the highest

The mortality rates in the urban districts were far greater than in the rural. The average urban death rate for the entire country was 338 7

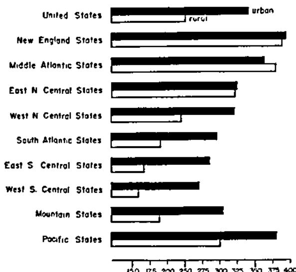


FIG 8.—DEATH RATE PER 100,000 POPULATION IN THE VARIOUS GEOGRAPHIC SUBDIVISIONS, UNITED STATES, 1940, URBAN AND RURAL DISTRICTS, COMPARED

while the rural death rate was 250 6 per 100,000 of the population. Here again we find considerable fluctuations in different sections of the country and in different states. In New York and New Jersey, for instance, the rural mortality rates even surpassed those of the urban. With these and a few other exceptions of individual states, however, the vast majority showed a *consistently* greater urban than rural death rate. In some, the difference was very marked. Thus, in Arizona, for instance, the urban death rate was 374 6 while the rural rate was only 136 5 per 100,000 of the population. A somewhat similar difference existed in Arkansas with death rates of 312 4 and 124 3 respectively for the urban and rural death rates.

It is interesting to observe that the death rates from heart disease in the

rural districts approach or surpass those of the urban regions only in the big industrial and commercial states It does not occur in thosestates where agriculture is the predominant industry. This may well be explained by the closeness of the rural districts to the great industrial centers and by the presence of industrialization in the rural districts. It may also partly be explained by the fact that the rural districts in these states being closer

TABLE 7.—*Death Rate from Circulatory Disease in Some of the Larger American Countries*

Country	*Year*	*Population*	*No of deaths*	*Rate per 100,000*
Argentina	1936	12,562,262	25,892	206 1
Canada	1944	11,958,000	31,746	265 5
Chile	1942	5,164,984	10,416	201 7
Colombia	1940	9,161,380	5,317	58 0
Mexico	1941	20,208,163	13,919	68 9
Peru	1943	7,045,687	3,068	43 5
Venezuela	1944	4,101,910	2,480	60 5

TABLE 8.—*Death Rate from Circulatory Disease in Large Countries in Other Parts of the World*

Country	*Year*	*Population*	*No of deaths*	*Rate per 100,000*
Australia	1943	7,229,864	23,211	321 0
Belgium	1944	8,251,576	25,850	313 3
Czechoslovakia	1937	15,239,000	36,614	240 3
England and Wales	1941	38,743,000	136,096	351 3
France	1942	37,700,000	105,552	280 0
Germany	1939	79,375,281	185,600	233 8
Hungary	1941	13,686,000	27,821	203 3
Italy	1942	45,414,491	102,305	225 3
Netherlands	1942	9,041,986	15,847	175 3
Norway	1941	2,959,961	4,644	136 9
Portugal	1944	8,043,315	14,496	180 2
Rumania	1939	19,933,802	29,910	150 0
Scotland	1943	5,157,000	16,809	325 9
Sweden	1942	6,432,337	17,405	270 6
Switzerland	1943	4,320,800	15,244	352 8

to the big cities, are inhabited in great part by industrialists and city workers.

The mortality rates from heart disease in other parts of the American continent[4] also show marked variations, as seen in Table 7. It will be observed that the death rates from heart disease are much lower in all these countries than the average death rate in the United States. This is undoubtedly due mainly to a greater mortality from infectious and contagious

diseases in these countries. A large portion of the population is thus carried off before it reaches the arteriosclerotic age. Another possible explanation is that the populations in these countries are smaller and spread out over wider areas. A third explanation may be the smaller consumption of food and more placid, carefree life of the natives who lack ambition and drive. Improper statistical recording of the causes of death may perhaps also be a big factor.

The mortality rates for other and more advanced countries approach those of the United States, as shown in Table 8.

Morbidity Incidence. The mortality rate from cardiovascular disease depicts the extent of the loss of human life but does not give us a true picture of the extent of morbidity and associated economic loss incident to such disease. Exact information on the morbidity incidence is not obtainable.

Some idea of the morbidity incidence may be gathered from a review of the records of nearly five million registrants for selective service in World War II, made by Eanes, McGill and Clark.[5] They estimated that 300,100 or 6.7 per cent had been rejected because of cardiovascular defects. The most frequent defects were rheumatic and luetic heart disease and arterial hypertension. It is interesting to find in their report that emergency workers, unemployed, and farmers showed the lowest percentage of such defects while students were in the highest percentage.

Inasmuch as the majority of this series consisted of comparatively young people, the incidence of cardiovascular disease in the general population would be expected to be far greater. Even on the basis of this incidence of 6.7 per cent, the number of sufferers from all forms of cardiovascular disease in the country in 1944, with an estimated population of 138,083,449, *might well have been over 9,000,000. With a mortality rate from all forms* of cardiovascular disease in 1944 of 433.6 per 100,000 the incidence of morbidity in relation to mortality would be 6,700 to 433.6 or about 16:1. In other words, for every person that died from cardiovascular disease, there were probably 16 others who continued living with a varying degree of physical handicap.

REFERENCES

[1] Vital Statistics, Federal Security Agency Vol. 25, No. 15, Nov. 22, 1946, Vol. 25, No. 5, June 7, 1946, Vol. 25, No. 6, June 26, 1946.
[2] Mortality Summary, Bureau of the Census, Vol. 16, No. 21, Aug. 12, 1942.
[3] Department of Commerce, Bureau of the Census, Washington, Yearly Estimated Population 1790 to 1946.
[4] Federal Security Agency, Int. List Nos. 90–103.
[5] Eanes, R. H., McGill, K. H., and Clark, M. L.: Cardiovascular defects in selective service registrants. Am. Heart J. 32: 504, 1946.

CHAPTER II

Etiology of Cardiovascular Disease

THE FUNDAMENTAL causes of cardiovascular disease and disturbances are varied and are the same as those of disease affecting other structures or organs of the body Indeed, in many cases, a given disease is not confined to the cardiovascular system alone, but other parts of the body are affected by it. Some disease states, however, have a predilection for the cardiovascular system in certain individuals.

Many of the causes of cardiovascular disease are still unknown. When, for instance, we speak of arteriosclerosis as a cause of heart disease, we are really speaking of a pathologic process of the arteries which results in the diseased state of the heart. Inasmuch as the causes of the arterial disease are, for the most part, unknown, the very fundamental causes of arteriosclerotic heart disease are not known. The same is true of hypertensive and of rheumatic heart disease

The causes of cardiovascular disease must, therefore, be considered from a broad aspect and may be divided into *intrinsic* and *extrinsic*. We shall attempt to describe these broader aspects in this chapter, leaving the discussions of the etiology of the specific forms of cardiovascular disease to later chapters.

INTRINSIC CAUSES

The intrinsic causes are constitutional in origin, and are predominantly hereditary. They may affect the cardiovascular system directly or through their influence on the nervous system, the endocrine glands, the metabolic state or the hemopoietic system

Direct Hereditary Effect The role of heredity in the causation of disease is often unappreciated, misunderstood or underestimated In its various manifestations, it may be considered to be the most important underlying cause of all disease

When we speak of an hereditary disease, we do not imply that the disease is actually transmitted from parent to offspring. The transmission may be in the form of a constitutional state which is susceptible to certain disease under given environmental conditions In other words, the hereditary units or genes which are transmitted for many generations from parent to offspring carry potential energies which, under given internal or external environmental influences, will result in certain bodily states, disease being one of them.

The kind of genes from which the individual develops is predetermined at sexual mating, not only by the immediate parents, but also by many generations back, each having some influence upon the given composition of the germ plasm To quote Bauer[1]: "Each individual *represents a host for the* germinal material, but in an ever new and never before existing combination of hereditary units, each of which was handed down to this particular individual from the previous generation"

The hereditary factor in cardiovascular disease may exhibit itself either in congenital maldevelopment or in a biologic inferiority of the cardiovascular system By the latter, we mean the inheritance of some intangible quality which predisposes the cardiovascular system to easy fatiguability, easy irritability, easy prey to destructive environmental conditions and to early senility or degenerative changes. Environmental factors, not enough to effect the heart or vascular system in most individuals, will readily undermine that of poor hereditary stock.

We frequently observe the occurrence of rheumatic heart disease, for instance, in certain families. Likewise, early development of arteriosclerosis *with special predilection to localized parts of the vascular tree such as the* coronary vessels has, in many cases, a family background. We all see instances of coronary sclerosis with the anginal syndrome and coronary thrombosis affecting comparatively young individuals in certain families, including grandparents, parents and two or more children, uncles, aunts and so on In some families, the predilection is to cerebral arteriosclerosis Many of these show signs of early aging. These individuals may have no more demonstrable provocative causes in life than the average normal individual. The environmental conditions may also be the same, yet the degeneration progresses at a rapid pace. Evidently, the inherited qualities of the cardiovascular system are such as to react excessively to whatever underlying causes there are that produce degeneration.

As will be shown in Chapter XVI, the causes of arterial hypertension are also still shrouded in mystery, except in those relatively few cases where the *condition can be traced to nephritis, a suprarenal tumor or other estab*lished causes. In the vast majority of cases where hypertension is of the so-called "essential" type, there is a definite hereditary background, with its recurrence in several generations in the same family Bauer feels that this vast group of cases should be labelled "constitutional" rather than "essential" hypertension.

Nervous and Psychosomatic Effect. With the advent of modern scientific medicine no field has been so sadly neglected as the study of the human personality in the causation or accentuation of disease We are so engrossed *in laboratory investigations of the causes and treatment of disease,* that we overlook the human and most important element which is respon-

sible in many cases for the various manifestations and expressions of abnormal bodily states This fact should be borne in mind especially by the recent graduate in medicine who is so conditioned in the details of laboratory diagnosis that he is apt to look at the patient as a mere test tube filled with chemicals, devoid of any sensitivity or feeling.

The subjective reaction of a given individual to a pathologic process in the body depends upon his particular response to irritation by such a process Witness, for instance, the reaction of different individuals to coronary insufficiency Many an autopsy is observed where the coronary vessels have been found almost entirely occluded by degenerative processes, yet there was no history of the anginal syndrome during life. In other cases with a history of angina pectoris of many years' standing, comparatively little may be found at autopsy to account for it. It stands to reason then that it is not the structural disease alone which is responsible for subjective manifestations but it is the individual reactivity to whatever abnormal processes that may exist in the body which makes one conscious of disease

The sensitivity of the nervous system varies greatly from person to person It depends upon the irritability of the central neurons and their response to impulses arriving there from various parts of the body. It is in the central neurons where the nervous impulses from various parts of the body are sifted, inhibited or accentuated in various degrees, depending upon the nervous makeup of the individual.

The psychologic makeup of the individual and his emotional reaction to internal and external environmental conditions are most important factors which determine the various manifestations of disease. In fact, in some cases, the emotional element is the only factor. Many a diseased state may be created by the conscious or subconscious mind and although such disease may not have an anatomico-pathologic background, it exhibits itself in sufficient physiologic disturbances to make it appear real. The subject will be dealt with more fully in Chapter XXVIII

Endocrinopathies. Functional abnormalities or imbalance of the endocrine glands are often potent causes of cardiovascular disturbances Outstanding examples are the abnormalities occurring in hypo- and hyperthyroidism and in hyperadrenalism with intermittent hypertensive crises in suprarenal tumors The marked acceleration of the heart and the rise in pressure on extreme emotional excitement are at least partly due to temporary increase in the outpour of adrenalin caused by sympathetic stimulation, as demonstrated by Cannon[2] There are undoubtedly many other cardiovascular disturbances due to endocrine dysfunction which are not fully known as yet Thus, vasomotor instability occurring at the meno-

pause is believed to be due to an increase of gonadotropic hormones in the blood, caused by the disappearance of estrogenic substances

Metabolic Disorders The known metabolic disturbances which are often associated with cardiovascular disease and may therefore be considered to be linked with the etiology of such disease are diabetes mellitus, gout and obesity. These conditions have definite hereditary predispositions

Diabetes mellitus is an endocrine disturbance, caused by diminished insulin secretion by the islands of Langerhans in the pancreas. The adrenals, pituitary and the nervous influence also play a part.

There is a definite relationship of this condition to early development of arteriosclerosis. How this relationship operates is not clear. Perhaps an associated disturbance in cholesterin metabolism frequently present in this disease is one of the factors which predisposes to arteriosclerosis In some of the milder cases of diabetes, developing after 40 years of age, the condition appears to be caused by arteriosclerosis rather than a cause of it. Degeneration of the islands of Langerhans probably takes place in such cases as a result of ischemia of the pancreas caused by local arteriosclerosis.

Gout is due to disturbances in the metabolism of purines. There is an elevation of the uric acid content of the tissue fluids, and late in the disease, salts of uric acid are deposited as tophi in certain parts of the body, especially in or about some joint In addition to many other possible complications, arteriosclerosis and hypertension are frequent accompaniments of this disease In 78 cases reported by Gudzent[3] all showed atheromatosis of the larger vessels at autopsy. The causal relationship of gout and arteriosclerosis is not known.

Severe obesity, whether of endocrine origin or due to a hereditary predisposition, often leads to early development of hypertension, arteriosclerosis and cardiac failure Individuals with this constitutional predisposition frequently have difficulty in reducing their weight even under the most rigid dietary discipline. The weight regulating mechanism is out of balance so that the utilization of food energy is greatly reduced This results in conversion of the various products into fat which is deposited in different parts of the body, especially the subcutaneous tissues Many patients have a severe craving for food, especially sweets, and habitually overeat

Disease of the Hemopoietic System: It is now well established that the primary anemias occur in individuals with a family predisposition to the disease. Secondary anemias are of course caused by an underlying disease such as malignancy, hemorrhage, severe prolonged infections and so on.

Any anemia, particularly the pernicious and sickle cell types, if severe enough and prolonged, will produce various cardiovascular disturbances.

It should therefore be considered an intrinsic etiologic cause of heart disease.

Extrinsic Causes

The extrinsic causes of cardiovascular disease are numerous and vary. They are infections, intoxications, mental or physical overwork, overindulgence in food on the one hand and insufficient and improper food on the other, poverty and ignorance with their associated unhygienic conditions, traumatic injuries and improper climate. All these factors play different roles in different individuals in producing diseased states and their manifestations In many cases, several etiologic factors are operative.

Infections The various infections and infectious diseases that may affect the cardiovascular system will be discussed later under appropriate headings Here, it may be said that almost every conceivable infection may directly or indirectly affect this system, to a varying extent. There are some infections, however, that have a predilection for this system, such, for instance, as rheumatic and syphilitic.

Intoxications: There are several substances which, if absorbed in large quantities and some even in small quantities, over a prolonged period are known to have direct or indirect toxic effects on the cardiovascular system. The most important of these are alcohol, tobacco, carbon monoxide, lead and benzene derivatives

Alcohol affects the nervous system mainly, but it also acts on the cardiovascular system. In small amounts it produces vasodilatation with beneficial effects in some vasospastic conditions In chronic alcoholic poisoning, brown atrophy of the heart with fatty infiltration may occur. Also, the production of arteriosclerosis is said to be promoted by chronic alcoholism, although this cannot be proven. Circulatory collapse may be observed in severe acute alcoholic poisoning.

Tobacco has been shown by Evans and Stewart[4] to decrease the blood flow, increase the blood pressure and pulse rate and decrease the skin temperature The last effect is due to vasoconstriction Its affect is indirect, through the autonomic nervous system I have observed cases presenting the anginal syndrome in mild form where the symptoms subsided on the cessation of smoking About 30 per cent of cases show slight transient changes in the electrocardiogram following heavy smoking, probably due either to mild coronary insufficiency or to vagosympathetic disturbance of the heart muscle induced by smoking

Carbon monoxide poisoning, such as that of illuminating gas or automobile exhaust gases, have their main toxic effect on the central nervous system, but the heart and blood vessels as well as other parts of the body may also

be involved. The heart often presents fatty degeneration and in some cases areas of necrosis. The walls of the smaller vessels often show swelling of the intima, fatty changes of the media, and arterial thrombosis is observed.

Lead poisoning, if chronic and long continued, may produce thickening of the media and periarteritis of the smaller arteries besides the changes in the kidney, liver, muscles, the anterior horn cells of the spinal cord and involvement of the peripheral nerves The incidence of hypertension and arteriosclerosis generally is said to be greater in individuals who are exposed to prolonged slow absorption of lead Its causal relationship to arteriosclerosis, however, has not been established and is being disputed.

Benzene poisoning, the chronic form, resulting from slow and prolonged absorption during contact with this product in industry, affects chiefly the circulating blood and blood forming tissues Anemia and leukopenia are

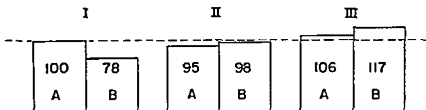


FIG. 9—RELATION OF OCCUPATION AND ECONOMIC STATUS TO THE MORTALITY FROM HEART

rectangle represents the mortality rate compared with that of all men and all married women taken as 100

the outstanding pathologic findings with associated symptoms of dizziness, weakness, palpitation and dyspnea on exertion Acute poisoning resulting from sudden inhalation of a high concentration of the product may result in unconsciousness and death.

Mental and Physical Overwork. Overwork, either mental or physical, and insufficient rest and relaxation, appear to be important contributing causes of cardiovascular disease. This is evidenced by the fact that workers in unskilled labor who are exposed to a great deal of physical strain, also professional men and leaders in industry who work under extreme mental and emotional strain, show the greatest incidence of heart disease This is illustrated by a statistical study of the mortality rate from heart disease in England and Wales during 1930 to 1932, as shown in Figure 9. It will be seen here that the death rate of skilled workers is smallest and that of unskilled laborers and professional men is greatest.

The accompanying graphs also show the effect of the economic status on the mortality rate It is best demonstrated by the death rate of women in the given groups. Wives of professional and executive groups have the lowest mortality rate while those of the unskilled and semiskilled group, the highest

Overfeeding Overindulgence in food is probably an important cause of diabetes, cardiovascular disease and other disturbances. A great many cases who suffer from hypertensive and arteriosclerotic heart disease as well as diabetes habitually overeat and carry an excessive amount of weight. Many of them partake of too much carbohydrates, fats, salt and cholesterin-containing foods It is a common experience to find a return of the blood sugar level to normal and the clearing up of a glycosuria in mild cases of diabetes on mere dietary care We also often observe a reduction in blood pressure in many hypertensive cases and symptomatic improvement of patients presenting cardiovascular disease by careful attention to diet and eating habits

Underfeeding This is just as important a cause of disease as overfeeding It lowers the resistance to infection and diminishes muscular and mental power This applies not only to a diminished caloric intake but also to a diminished intake of the required amount of proteins, fats, carbohydrates and the various vitamins Vitamin B deficiency particularly has in recent years been recognized as a direct underlying cause of some forms of cardiac disease

Poverty and Ignorance These two factors are very potent predisposing causes of disease generally, including cardiovascular disease Improper nutrition, poor ventilation and lack of sunshine in living quarters, overcrowding, filth and improper or insufficient clothing are all predisposing causes of infections and infectious disease It is common experience of all practicing physicians to find the greatest incidence of rheumatic heart disease and other infectious states under such conditions Swift,[5] in his study of a large series of cases of rheumatic fever, found its incidence to be about fifteen to twenty times more frequent among poor classes than in the well to do

Climatic Conditions The effect of climate on the production of disease is often not fully appreciated The relative amount of humidity, sunshine, the average atmospheric pressure and temperature, the amount of rainfall and wind in different parts of the country are all important factors in promoting health or in the production of disease These various factors are probably partly responsible for the variations in the mortality rate in different parts of the country, described in Chapter I.

A cold, moist, and even a cold, dry climate, is not well borne by elderly

arteriosclerotic and generally debilitated individuals. In the presence of coronary disease, it is often observed that the anginal syndrome develops on leaving a warm house and on attempting to walk on the street, especially in cold or windy weather. The same individual is often perfectly free from pain when working or walking around indoors, or when he moves to a warm climate.

A cold, moist climate is also very bad for individuals having a predisposition to rheumatic fever and to various other joint diseases. Perspiration is checked and there is a tendency to vascular stasis and to activation of various dormant foci of infection. Swift found that the temperate zone favors the development of rheumatic fever in the winter Tropical sections as well as dry summer weather in other areas inhibit or prevent its evolution.

High altitudes increase the respiratory and circulatory rates to compensate for the rarefaction of oxygen in the air The higher the altitude, the greater such rarefaction and therefore the greater the burden on the circulation and respiration. In nature's attempt to overcome the oxygen deficiency, a compensatory increase in the number of red blood cells and hemoglobin takes place This, as well as the increase in circulation rate, may seriously affect an individual with hypertension or with arteriosclerotic heart disease. Conditions of this kind, however, may be excellent for the anemias, general debility, neurasthenias, tuberculosis and in physical states where the expansion of the lungs is poor.

Impurity of air is an important factor in the production of symptoms of cardiovascular disease Big cities, especially factory districts, where there is a considerable amount of soot, dust and noxious gases in the air are often bad places for sufferers from such disease. The author has observed on many occasions persons with coronary disease who suffered considerably from the anginal syndrome while in the city and who were entirely free from symptoms in their country homes and environment He has in mind a patient who could not walk more than one block in the city without great discomfort, but who could walk a considerable distance, even uphill, without any disturbance, in the open country a great distance from any factories, automobile roads and habitation. Of course the restful and relaxing country environment is also a factor.

REFERENCES

[1] Bauer, J.. Constitution and Disease New York, Grune & Stratton, 1942

[2] Cannon, W. B. Bodily Changes in Hunger, Fear, Pain, Rage London and New York, D Appleton Co, 1915.

[3] Gudzent, F.· Gicht und Rheumatismus Berlin, Julius Springer, 1928, p 189

[4] Evans, W F, and Stewart, H. J: The effect of smoking cigarettes on peripheral blood flow Am Heart J. 26 78, 1943.

[5] Swift, H. F.: Factors favoring the onset and continuation of rheumatic fever. Am Heart J 6:625, 1930–31.

CHAPTER III

Essential Anatomic Features of the Cardiovascular System

In order to understand the pathologic changes that occur in disease of the circulation, it is essential to review briefly the normal anatomic highlights of the cardiovascular system This chapter attempts such a review Of course, only the briefest outline is possible in a treatise of this kind For more detailed discussion, the student is referred to textbooks on anatomy.

General Survey

The cardiovascular system is a closed circuit of vessels, the central organ of which is the heart Leading from the right ventricle is the pulmonary artery and from the left, the aorta These send off branches which divide and subdivide into innumerable arteries and arterioles, finally ending in a capillary network These are then continued by venules which combine to form larger veins and these in turn into still larger ones, ultimately joining to form the superior and inferior venae cavae, which enter the right auricle and the four pulmonary veins which enter the left auricle A diagrammatic representation of the circulation is shown in Figure 10.

The entire cardiovascular system has one common layer of cells—the endothelial layer—which lines the inner portion, thus forming one continuous closed system of tubes In the capillary portion, which is in direct contact with all body tissues, the endothelium is the only layer. The rest of the cardiovascular system is composed of three coats, the innermost of which is lined by the endothelial layer. The thickness of each coat varies with the different parts of the cardiovascular system and depends upon the predominant function of the given part Thus, the heart, functioning as a pump, consists predominantly of myocardium or muscular tissue, covered by thin inner and outer linings—the endocardium and pericardium respectively. In the arteries, arterioles, venules and veins, the intima or inner coat, media or middle coat and adventitia or external coat consist of various layers of cells. The thickness of each layer varies in the different vessels according to the main function of the given vessel. The intima generally consists of the endothelial layer, subendothelial connective tissue and an elastic membrane. The media consists predominantly of muscle fibers disposed circularly around the vessel wall as well as some elastic fibers The adventitia consists predominantly of connective tissue and elastic fibers.

Since the largest arterial trunks, the aorta and pulmonary artery, have as their main function the sudden stretching and rebound of their walls, they contain a predominance of elastic tissue in all three coats, as shown in

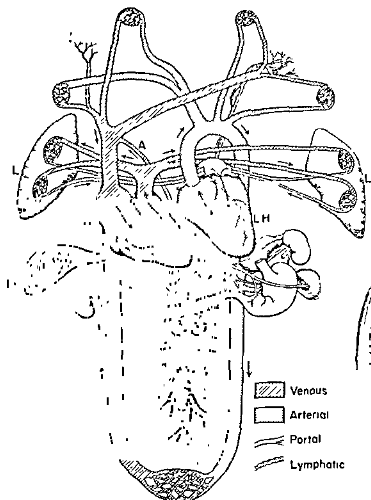


FIG 10—SCHEMATIC REPRESENTATION OF CIRCULATION. For simplicity, the heart is separated into a right heart, RH, and left heart, LH. Direction of blood flow is shown by arrows L, lungs, Lr, liver; A, azygos vein emptying into superior vena cava See text

Figure 11. In the aorta, this is much more marked than in the pulmonary artery because *of greater pressure occurring in the former during life*, as will be shown later. For this reason also, the aortic wall is thicker than the wall of the pulmonary artery. In the smaller arteries, the elastic and

CHAPTER III

Essential Anatomic Features of the Cardiovascular System

In order to understand the pathologic changes that occur in disease of the circulation, it is essential to review briefly the normal anatomic highlights of the cardiovascular system This chapter attempts such a review. Of course, only the briefest outline is possible in a treatise of this kind For more detailed discussion, the student is referred to textbooks on anatomy.

General Survey

The cardiovascular system is a closed circuit of vessels, the central organ of which is the heart. Leading from the right ventricle is the pulmonary artery and from the left, the aorta. These send off branches which divide and subdivide into innumerable arteries and arterioles, finally ending in a capillary network These are then continued by venules which combine to form larger veins and these in turn into still larger ones, ultimately joining to form the superior and inferior venae cavae, which enter the right auricle and the four pulmonary veins which enter the left auricle A diagrammatic representation of the circulation is shown in Figure 10

The entire cardiovascular system has one common layer of cells—the endothelial layer—which lines the inner portion, thus forming one continuous closed system of tubes In the capillary portion, which is in direct contact with all body tissues, the endothelium is the only layer. The rest of the cardiovascular system is composed of three coats, the innermost of which is lined by the endothelial layer The thickness of each coat varies with the different parts of the cardiovascular system and depends upon the predominant function of the given part. Thus, the heart, functioning as a pump, consists predominantly of myocardium or muscular tissue, covered by thin inner and outer linings—the endocardium and pericardium respectively In the arteries, arterioles, venules and veins, the intima or inner coat, media or middle coat and adventitia or external coat consist of various layers of cells. The thickness of each layer varies in the different vessels according to the main function of the given vessel. The intima generally consists of the endothelial layer, subendothelial connective tissue and an elastic membrane. The media consists predominantly of muscle fibers disposed circularly around the vessel wall as well as some elastic fibers. The adventitia consists predominantly of connective tissue and elastic fibers.

connective tissue portions are greatly diminished and the muscular layer in the media is relatively greater, as shown in Figure 12. The adventitial layer *gradually dwindles and finally entirely* disappears as the capillaries are approached. The relative preponderance of the muscular layer in the media of the smaller vessels corresponds to the function of contraction and dilatation of these vessels



FIG 13 —SECTION OF THE TONGUE OF A RAT WITH INJECTED ARTERIOLES AND CAPILLARIES, ILLUSTRATING THE GREAT NETWORK OF THE CAPILLARIES × 150

The capillary vessels, as shown in Figure 13, are composed of a single endothelial layer of cells joined edge to edge by an interstitial cement substance. This structural arrangement conforms with the function of the capillaries in the interchange of materials between the blood and all the body cells The greater the activity of an organ, the greater is its capillary network and therefore the larger its blood supply

In the veins, Figure 12, the three coats are comparatively thin and in the small veins they are hardly distinguishable The caliber and number of veins in the systemic venous system is larger than that of the arteries. Hence, the total capacity of the venous system is much greater than that

of the arterial system. The pulmonic venous system approximates in capacity that of the pulmonic arterial system.

To prevent backflow of blood in the systemic venous system, many of the larger veins are provided with valves. These are especially numerous in the veins of the lower extremities where the effect of gravity, which tends to interfere with venous return, is greatest

The veins have much greater communication with one another than the arteries Especially marked anastamosis exists among the venous sinuses of the cranium and among veins of the neck, vertebral canal and the various plexuses of the abdomen and pelvis

Of special interest in the venous system is the portal vein. This vein carries the venous blood from the spleen and from the viscera of digestion to the liver, shown diagrammatically in Figure 10. In the substance of the liver it ramifies into a network of capillary-like vessels which then reassemble to form the hepatic vein, carrying the blood into the inferior vena cava. The portal venous system is thus unique in originating in a system of capillaries and again ending in capillaries The products of digestion are thus conveyed to the liver for its various metabolic changes, purification and detoxification.

Closely connected with the cardiovascular system, and to be considered part of it because of its function in the movement of the body fluids, is the *lymphatic system*. This consists of a capillary network and larger lymphatic vessels. The capillary network is widespread throughout the body, invading every tissue and organ. The larger lymphatic vessels are interspaced by lymph nodes which act as filtering organs and supply lymphocytes to the lymph

The lymphatic vessels draining the right side of the head, neck and thorax, right upper extremity, right side of the heart and convex side of the liver lead to the right lymphatic duct which empties into the right subclavian vein at its junction with the right internal jugular. The lymphatic vessels from all the rest of the body lead to the thoracic duct which empties into the venous system, at the junction of the left internal jugular and left subclavian veins. These are illustrated diagramatically in Figure 10.

The movement of the lymph from the lymphatic capillaries towards the venous system is accomplished by the contraction of the lymphatic vessels. In the mesentery of the rat, such contractions have been observed to occur at a rate of twelve to eighteen times per minute in each segment. To prevent the backflow of the lymph, the vessels contain numerous valves which give them a beaded appearance

The lymphatic vessels leading from the small intestines carry the chyle during the process of digestion They are therefore known as lacteals or chyliferous vessels.

We shall now proceed with a more detailed description of the important parts of the cardiovascular system.

The Heart

The normal heart is a somewhat conical-shaped organ, varying in size and appearance with the constitutional build, age and sex of the individual In the adult it is about 12 centimeters long, 8 to 9 centimeters wide at its broadest portion, and 6 centimeters thick

Table 9 —*Normal Weight of the Heart (Male and Female)*

Pounds		Kilograms		Body Weight Minimum Gm		Average Gm		Maximum Gm	
M	F	M	F	M	F	M	F	M	F
105	90	47	40	165	135	205	162	241	193
110	95	50	43	173	143	215	171	253	204
115	100	52	45	181	150	225	180	264	215
120	105	54	47	190	158	235	189	276	226
125	110	56	50	198	165	245	198	287	237
130	115	58	52	206	176	255	207	299	248
135	120	60	54	213	180	265	215	310	259
140	125	63	56	221	188	274	225	322	268
145	130	65	58	229	195	284	234	333	277
150	135	68	60	237	203	294	244	345	286
155	140	70	63	245	211	304	253	356	295
160	145	72	65	253	219	313	262	368	304
165	150	74	68	261	225	323	272	370	313
170	155	77	70	268	233	333	282	371	322
175	160	79	72	280	240	343	288	372	330
180	165	81	74	288	247	353	297	373	337
185	170	83	77	296	255	363	306	382	343
190	175	86	79	304	283	373	315	392	350
195	180	88	81	312	301	382	324	402	356
200	185	90	83	320	309	392	333	412	361
	190		86		317		342		366
	195		88		325		351		371

Weight The normal weight of the heart in the adult varies, according to Smith,[1] between 165 and 412 grams, the average being 294 for males, and 250 for females

ratio is somewhat higher than in fat individuals. In predicting the approximate normal weight of the heart in grams, we may therefore multiply the body weight in kilograms by 4 3 in males and 4 0 in females, with an error varying from 8 to 10 per cent. Table 9 presents the minimum, average and maximum weight of the heart for different body weights in males and fe-

males, as determined by Smith, and presented in a condensed form in the "Nomenclature for Diagnosis" of the New York Heart Association.

In infancy and childhood, the weight of the heart varies between 20 and 25 grams the first 6 months, 30 to 40 grams the first year, and gradually increases till it reaches about 95 to 105 grams at 8 years of age Between 12 and 16 years it varies between 150 to 250 grams. The ratio of heart weight to body weight is much greater in infancy and childhood than in adults and gradually approaches the adult ratio as age advances.

Position in the Chest. The heart is suspended in the mediastinum from the great arterial and venous trunks which enter and leave its chambers It is enveloped by the pericardium. Its base is directed upwards, backwards and to the right and is made up of the left auricle and a small part of the right auricle The apex is directed downwards, forwards and to the left The sterno-costal surface consists of parts of the right auricle and right ventricle and a narrow strip of the left ventricle. The diaphragmatic surface embraces portions of the two ventricles and rests upon the central tendon and adjacent portion of the left dome of the diaphragm.

The Pericardium The heart and the roots of the great vessels arising from it are enclosed by a flasklike sac, the *parietal pericardium.* The pericardium consists of an outer fibrous and inner serous layer Its upper part is narrowed in the form of a neck, where the fibrous layer completely encloses the sac by its fusion with the coats of the great vessels and is continuous with the pretracheal layer of the deep cervical fascia. It has firm attachments by ligaments to the posterior surface of the manubrium sterni and to the xyphoid. It also fuses with the central tendon of the diaphragm and is attached to part of the left dome The heart, which is suspended in the parietal pericardium, thus receives considerable support. The inner or serous layer of the *parietal pericardium* is reflected on the heart and covers its entire surface. The part covering the surface of the heart is known as the *visceral pericardium.* Figure 14 shows the front view of the heart.

Chambers and Their Openings: The right auricle is larger than the left and its wall is thinner, measuring about 2 millimeters It may hold 57 cc of blood Opening into it are the superior venae cavae in the upper and posterior part; the inferior venae cavae, in the lowest part, near the septum; the coronary sinus and the thebesian vessels. Leading from the right auricle to the right ventricle is the auriculo-ventricular orifice guarded by the tricuspid valve. This orifice is 4 centimeters in diameter and is surrounded by a fibrous ring.

The right ventricle is of triangular shape. The lower surface is flattened and rests upon the diaphragm. The posterior wall consists of the interventricular septum which bulges somewhat into the right ventricle. The

upper left angle forms a pouch, the *conus arteriosus*, from which the pulmonary artery arises In size, the right ventricular cavity is the same as the left It may hold 85 cc. of fluid. The thickness of its wall is normally about 5 millimeters or less Figure 15 shows interior of right ventricle.

The left auricle is smaller than the right, but its wall is thicker, measuring about 3 millimeters It is concealed in front by the pulmonary artery and

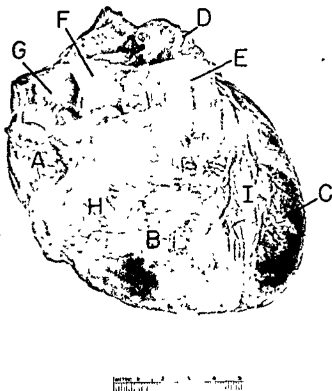


Fig 14—Front View of the Heart A, right auricle, B, right ventricle, C, left ventricle, D, edge of left auricle, E, stump of pulmonary artery, F, stump of aorta; G, stump of superior vena cava, H, coronary sulcus, I, anterior longitudinal sulcus

aorta The two right pulmonary veins enter on its right side; the two left, on its left side. The left auriculo-ventricular orifice is smaller than the right and is surrounded by a dense ring. It is situated below and to the left of the aortic orifice. Its valve, the mitral valve, is bicuspid, consisting of an anterior and a smaller posterior leaflet.

The left ventricle is larger than the right, its walls being about two and one-

half times as thick, but its thinnest part at the apex measures only 2 to 3 millimeters. Figure 16 shows the inner part of the left ventricle.

Muscular Architecture. In the auricles there are two main layers of muscle. The superficial layer appears to originate from the orifice of the superior vena cava and from the anterior part of the auricular septum.



Fig. 15.—Inner View of the Right Ventricle. Anterior wall of right ventricle sectioned and deflected showing the semilunar valves and parts of the tricuspid valve.

From here, it radiates in the form of muscle bundles covering both auricles and ends in the area of their origin. A deeper longitudinal layer is confined chiefly to each chamber. These two layers merge into one another.

In the *ventricles* there exist several distinct groups of muscle bundles. Mall[2] has clearly shown the presence of well marked lines of separation between these various bundles. The fibers of each muscle bundle run in

parallel directions, although a considerable amount of interlacing of fibers occurs among the various bundles.

Robb[3] and Robb and Robb[4] in more recent studies have clearly outlined these muscle layers and have demonstrated the presence of connective tissue sheaths as well as independent blood vessels and Purkinje strands for each muscle.

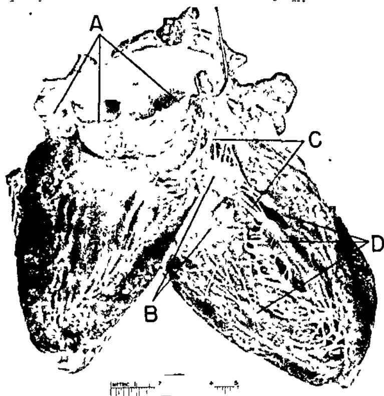


FIG 16—INNER VIEW OF THE LEFT VENTRICLE Ventricle has been opened so as to visualize the semilunar valve of the aorta, A, and the mitral valve, B, the anterior leaflet of which is deflected The chordae tendineae, C, and the papillary muscles, D, are visualized

muscles.

The superficial sinospiral muscle, Figure 17, arises from the right auriculoventricular ring. The superficial bulbospiral muscle, Figure 18, arises

from the conus tendon, left trigonum fibrosum and from the left auriculo-ventricular ring. The two muscles run spirally downwards, towards the apex Here, they form a vortex, penetrate the interior of the ventricles, continue subendocardially upwards towards their point of origin at the base, and are inserted into the tendons of the auriculo-ventricular orifice in each ventricle. Many of the muscle fibers are inserted directly in those tendons. Others form the papillary muscles from which the chordae tendineae arise, and are attached to the valve leaflets, which in turn are inserted in the tendon of the given auriculo-ventricular ring.

The deep sinospiral muscle, Figure 19, has two points of origin from the auriculo-ventricular ring In the posterior interventricular groove, it splits into a deep layer covering the ventricle and a more superficial layer, covering the lateral wall of the right ventricle. The deep bulbospiral muscle, Figure 20, is confined only to the left ventricle. Its origin and insertion are in the septal curve of the mitral ring It has three interweaving bands surrounding the mitral and aortic orifices

The three scroll muscles take their origin in the papillary region of one ventricle, wrap themselves around that ventricle and pass diagonally, forming the interventricular septum, and turn back to the wall of the other ventricle In so doing, these three muscles form an elaborate S shaped enclosure of the two ventricular cavities and constitute the interventricular septum The scroll muscles are enclosed by the sinospiral and bulbospiral muscles.

The fourth or "cuff" muscle is a heavy muscle layer confined only to the left ventricle

From the anatomic locations, origins, and insertions of the various muscle layers of the heart, we may assume that each group has a specific function during systole, as is stressed by Robb and Robb. The superficial and deep sinospiral and bulbospiral muscles tend to approximate the apex to the base. The scroll muscles narrow the ventricular cavities. The cuff muscle completes the expulsion of blood into the aorta The interventricular septum is thus not merely a wall separating the two ventricles but actually participates in ventricular contraction and in the narrowing of the cavities of the ventricles. Also, the papillary muscles are not independent structures but are parts of the origin and insertion of the various muscular layers

Histologic Features The ventricular muscle cells are irregular in shape, somewhat rhomboidal, and frequently divide into branches which join with adjacent cells. There is no sarcolemma. As in voluntary muscles there are transverse striations present. Although the fibers seem to form a syncytial arrangement, they assume in the main, a definite parallel arrangement in given sections, as shown in Figure 21.

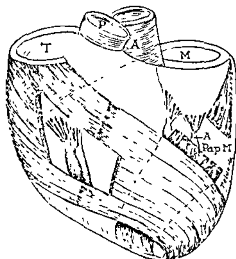


FIG 17 —SUPERFICIAL SINO-SPIRAL MUSCLE, SEEN FROM THE ANTERIOR SURFACE OF THE HEART T, tricuspid orifice, P, pulmonary artery, M, mitral orifice, A, aorta

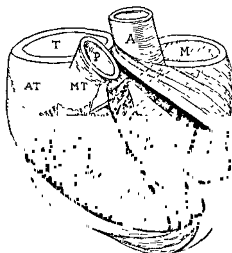


FIG 18 —SUPERFICIAL BULBOSPIRAL MUSCLE AT, anterior leaflet and MT, medial leaflet of tricuspid valve, post leaf, posterior leaflet of tricuspid valve

According to Cohn,[5] the number of muscle fibers in the heart probably does not change from birth to death but there is an alteration of the intimate structure of fibers as age progresses. At beginning of life a muscle cell contains very little besides an ovoid globular nucleus. The cross

from the conus tendon, left trigonum fibrosum and from the left auriculo-ventricular ring The two muscles run spirally downwards, towards the apex Here, they form a vortex, penetrate the interior of the ventricles, continue subendocardially upwards towards their point of origin at the base, and are inserted into the tendons of the auriculo-ventricular orifice in each ventricle Many of the muscle fibers are inserted directly in those tendons Others form the papillary muscles from which the chordae tendineae arise, and are attached to the valve leaflets, which in turn are inserted in the tendon of the given auriculo-ventricular ring

The deep sinospiral muscle, Figure 19, has two points of origin from the auriculo-ventricular ring In the posterior interventricular groove, it splits into a deep layer covering the ventricle and a more superficial layer, covering the lateral wall of the right ventricle. The deep bulbospiral muscle, Figure 20, is confined only to the left ventricle. Its origin and insertion are in the septal curve of the mitral ring It has three interweaving bands surrounding the mitral and aortic orifices

The three scroll muscles take their origin in the papillary region of one ventricle, wrap themselves around that ventricle and pass diagonally, forming the interventricular septum, and turn back to the wall of the other ventricle In so doing, these three muscles form an elaborate S shaped enclosure of the two ventricular cavities and constitute the interventricular septum The scroll muscles are enclosed by the sinospiral and bulbospiral muscles

The fourth or "cuff" muscle is a heavy muscle layer confined only to the left ventricle

From the anatomic locations, origins, and insertions of the various muscle layers of the heart, we may assume that each group has a specific function during systole, as is stressed by Robb and Robb The superficial and deep sinospiral and bulbospiral muscles tend to approximate the apex to the base The scroll muscles narrow the ventricular cavities The cuff muscle completes the expulsion of blood into the aorta. The interventricular septum is thus not merely a wall separating the two ventricles but actually participates in ventricular contraction and in the narrowing of the cavities of the ventricles. Also, the papillary muscles are not independent structures but are parts of the origin and insertion of the various muscular layers.

Histologic Features: The ventricular muscle cells are irregular in shape, somewhat rhomboidal, and frequently divide into branches which join with adjacent cells. There is no sarcolemma As in voluntary muscles there are transverse striations present. Although the fibers seem to form a syncytial arrangement, they assume in the main, a definite parallel arrangement in given sections, as shown in Figure 21.

discs, and steplike concentrations appear, while the nucleus becomes cloudy. Later, spaces filled with lypochrome pigment appear at the nuclear poles.

Conduction System: This is a special system of neuro-muscular structure connecting the auricles and ventricles It consists of the sino-auricular node, the auriculo-ventricular node, the bundle of His, and its two bundle branches, which break up into the Purkinje system of fibers running subendocardially throughout the ventricular musculature. These were fully described elsewhere[6]



FIG. 21 —HISTOLOGIC STRUCTURE OF THE HEART MUSCLE, HIGH MAGNIFICATION X 500

Glomset and Glomset[7] and Glomset and Birge[8] expressed doubt as to the actual presence of a conduction system in man. In the literature, they found considerable contradictory reports as to the location, size and structure of the sinoauricular node. Their studies indicate that the various structural components of the node such as nerve trunks, groups of ganglion cells and the slender muscle fibers, are present not only in the area where the node is supposed to be but in many areas of the auricles, especially at the venous openings, and also in the ventricles In addition, they found many muscular bridges between the auricles and ventricles in the auriculoventricular groove. They did find an easily recognizable sinus node as

well as the bundle of His and the two bundle branches in cattle, sheep, and hogs. Here, the bundle and its branches are surrounded by a distinct sheath of connective tissue which is easily made evident by injection of colored materials. Even in these animals, however, the auriculo-ventricular node is situated, according to these authors, not in the lower right auricle but on the top of the ventricular muscle septum near the posterior part of the central fibrous body The node was not found to be connected with the auricular muscle fibers. In man and dog, a search in the homologous portion of the heart did not appear to reveal a conduction system. Cells of the Purkinje type were found scattered in isolated areas of the auricular and ventricular musculature.

On the other hand, the authors observed an extremely well developed intrinsic nervous system of the heart, consisting of nerve cells, trunks, networks of nerve fibers and ganglia, most prevalent in the auricles and the auriculo-ventricular groove

If these findings are corroborated by further investigation, our present concept of the origin and propagation of the cardiac impulse will have to be modified

The Main Vascular Trunks

The Superior Vena Cava: The superior vena cava is 7 centimeters long and is formed by the union of the two innominate veins. It begins at a level of the cartilage of the first right rib, close to the sternum, descends vertically downwards, and ends in the right auricle at the level of the upper border of the third costal cartilage.

The Inferior Vena Cava. This is formed in the abdomen by the union of the two common iliac veins. It runs upwards along the front of the vertebral column at the right side of the aorta, continues in the groove of the posterior surface of the liver, and enters the chest through the perforation in the central tendon of the diaphragm In the chest it extends for a distance of about 2 5 centimeters, pierces the fibrous pericardium, and enters the lower and back part of the right auricle It possesses a rudimentary valve at its opening in the auricle.

When the inferior vena cava is obstructed the venous blood from the abdomen, pelvis, and lower extremities returns to the heart mainly by the *azygos* and *hemiazygos* veins which connect the tributaries of the inferior vena cava, the common iliac and ascending lumbar veins with the superior vena cava.

The Pulmonary Artery This artery carries the venous blood from the right ventricle to the pulmonary fields. It is about 5 centimeters long and 3 centimeters in diameter It arises from the conus arteriosus of the right

ventricle and runs, in an upwards and backwards direction, first to the front then to the left of the ascending aorta It divides under the arch of the aorta into the right and left branches.

The right branch runs behind the ascending aorta and superior vena cava and in front of the right bronchus to the root of the right lung. There, it divides into two branches—an upper to the upper lobe and a lower to the middle and lower lobes of the right lung. The left branch runs horizontally in front of the descending aorta and left bronchus to the root of the left lung, where it divides into two branches: one to the upper and the other to the lower lobes of the left lung

In the lungs, these main branches divide into numerous sub-branches, finally ending in a capillary network which is the richest in the body. They line the epithelium in the walls of the alveoli. The pulmonary veins originate in the pulmonary capillaries of the alveoli. About twenty-five capillary loops intervene between the arterial and venous radicals. The venules combine into larger veins which ultimately end in the four venous trunks which empty into the left auricle.

The blood supply to the lungs, bronchi, bronchial glands, interlobular arealar tissue, pleural surfaces and pulmonary vessel walls is not derived from the pulmonary circulation but from the bronchial arteries These originate either in the upper part of the thoracic aorta or from the upper aortic intercostal arteries. The venous return links up with the bronchial veins formed at the root of the lungs. These end in the azygos and hemiazygos veins A large part of the blood returns by the pulmonary veins

Pulmonary Veins: The four pulmonary veins, two from each lung, open into the posterior part of the left auricle

The Aorta: This consists of an ascending portion, an arch, and a descending portion.

The *ascending* portion arises from the left ventricle at the level of the third left costal cartilage. It curves obliquely upwards, anteriorly and to the right, to the level of the upper border of the second right costal cartilage It is about 5 centimeters long and lies 6 centimeters behind the sternum. Close to its origin, it gives rise to the two coronary arteries

The arch forms a curve and runs obliquely upwards, backwards, and to the left, first in front of, then to the left of the trachea. Reaching the left side of the fourth thoracic vertebra, it again forms a curve and runs downwards as the descending aorta The upper part of the arch is usually about 2.5 centimeters below the superior border of the manubrium sterni In occasional cases, it may reach the top of the manubrium, and in rare cases, it may be 5 to 8 centimeters below.

There are four nerves which come in close relation with the arch of the

aorta and which play a role in the production of symptoms and signs of aneurysms of this part of the aorta They are the left phrenic, the lower superior cardiac branch of the left vagus, the superior cardiac branch of the left sympathetic, and the trunk of the left vagus This last nerve crosses the arch and gives rise to the recurrent laryngeal nerve, which hooks around below the vessel and then passes upwards on its right side.

There are three branches springing from the arch: the innominate, the left common carotid, and the left subclavian arteries.

The innominate is 4 to 5 centimeters long It arises at a level of the upper border of second right costal cartilage and extends to the right sternoclavicular articulation where it branches off into the right common carotid and right subclavian arteries.

The left common carotid artery springs from the highest part of the arch, to the left of the innominate. It extends to the left sternoclavicular articulation and continues into the cervical region

The left subclavian artery arises behind the left common carotid at the level of the fourth thoracic vertebra It extends to the root of the neck and then arches laterally

The *descending aorta* consists of a thoracic and an abdominal portion The thoracic portion is situated in the posterior mediastinum, to the left of the spinal column, but gradually curves toward the right, approaching the median line as it enters the abdomen through the aortic hiatus in the diaphragm It is continued as the abdominal portion to the fourth lumbar vertebra where it divides into the two common iliac arteries. In the thorax, its main branches are the pericardial, bronchial, esophageal, mediastinal, intercostal, subcostal and superior phrenic The main abdominal visceral branches are the celiac, superior mesenteric, inferior mesenteric, middle suprarenals, renals, internal spermatic, and ovarian. The parietal branches are the inferior phrenic, lumbars, and middle sacral

The Coronary Blood Vessels The blood supply to the heart is carried by the two main coronary arteries, which spring from the sinus of Valsalva in the first part of the ascending aorta

The *right coronary artery* reaches the surface of the heart between the right auricle and the conus arteriosus and proceeds to the right in the auriculo-ventricular groove, to reach the posterior surface of the heart, where it usually descends in the posterior interventricular groove as the posterior descending branch, terminating at the apex According to Barnes and Whitten[9] the numerous branches given off by this artery supply two thirds of the anterior and all of the posterior surface of the right ventricle. In those cases, in which a posterior descending branch is present, this branch supplies part of the interventricular septum and in many

cases about one-half of the basal and three-fifths of the posterior wall of the left ventricle.

The left coronary artery, soon after it reaches the surface of the heart, divides into two branches—the anterior descending and the circumflex

The anterior descending branch runs in the anterior interventricular groove down to the apex where it usually swings around to the diaphragmatic surface of the left ventricle and disappears in the muscle wall after breaking up into many subdivisions Numerous large lateral branches are given off by this artery. These branches supply the anterior and lateral parts of the wall of the left ventricle, the anterior part of the interventricular septum and part of the right ventricle.

The circumflex branch swings around to the left in the auriculo-ventricular groove and reaches the posterior or diaphragmatic surface of the left ventricle. In many cases, it descends in the posterior interventricular groove down to the apex as the posterior descending branch. The first portion which runs in the auriculo-ventricular groove, supplies branches to the left auricle and the lateral part of the left ventricle. The posterior descending portion, where present, sends off many branches, which supply the posterior surface of the left ventricle, the posterior interventricular septum and part of the right ventricle.

There are considerable variations in the patterns of the coronary blood vessels in different individuals. Using a modified Gross[10] method of roentgenographic study of the heart in which the coronary vessels were injected with a special radio-opaque substance and the heart was unrolled, Schlesinger[11] observed three main groups of variations. Each of these groups is based on the predominance of the right or left coronary artery in the supply of blood to the posterior surface of the heart in the location where the left and right auricles and ventricles and their septae meet. This area is known as the crux. In Group I, Figure 22, the right coronary artery predominates in its supply to this area. In Group II, Figure 23, both coronaries supply equally to this area. In Group III, Figure 24, the left coronary predominates in its supply. These variations play important parts in the determination of the extent of infarction in this area of the heart in occlusion of a given coronary vessel, as will be discussed in Chapter XIX.

The smaller arterial branches penetrate the muscle wall and break up into arterioles. According to Robb and Robb[4] each muscle layer has its own arterial supply. The arterioles lie in the spaces between the muscle bundles. Just before an arteriole breaks up into capillaries, it penetrates the muscle bundle. The capillary network thus formed supplies the individual muscle fibers, each fiber lying in contact with one or more capillaries.

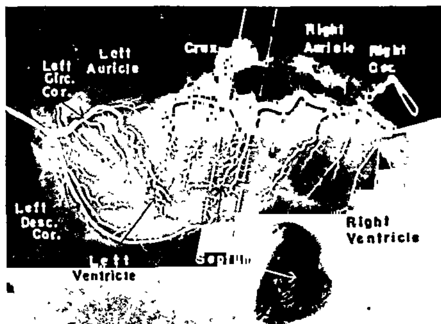


Fig 22 —Coronary Arteries in the Human Heart Group I where the right coronary artery predominates in its supply to the crux.



Fig 23 —Coronary Arteries in the Human Heart. Group II where both the right and left coronary arteries predominate in their supply to the crux.

The venules and veins draining the tissues of the heart, empty mainly into the right auricle through the coronary sinus, but the great posterior cardiac veins also participate in returning of the venous blood. By means of the free intercommunication of the cardiac veins with the thebesian veins, a good portion of the venous blood empties through the latter into the right ventricle and to a very slight degree also into the left ventricle



FIG 24 —CORONARY ARTERIES IN THE HUMAN HEART. Group III where the left coronary artery predominates in its supply to the crux (Courtesy of Dr. Schlesinger and the American Association for the Advancement of Sciences)

A more complete description of the coronary circulation is given elsewhere [5]

REFERENCES

[1] Smith, H L: The relation of the weight of the heart to the weight of the body and of the weight of the heart to age. Am Heart J 4 79, 1928–29

[2] Mall, F P On muscular architecture of the ventricles of the human heart. Am J. Anat 11 211, 1910–11.

[3] Robb, J S The role of muscle bundles in ventricular conduction Medical and Surgical Year Book, Phys. Hospital, Pittsburgh 1 210, 1929

[4] ——, and Robb, R C. The normal heart, anatomy and physiology of the structural units Am Heart J 23 455, 1942.

[5] Cohn, A. E Disease of the heart. Science 101 499, 1945

[6] Sigler, L H The Electrocardiogram: Its Interpretation and Clinical Application New York, Grune & Stratton, 1944 Pp 5-7
[7] Glomset, D J, and Glomset, A T A Morphologic study of the cardiac conduction system in ungulates, dog and man Am Heart J 20 389, 1940; ibid 20 677, 1940
[8] ——, and Birge, R F A morphologic study of the cardiac conduction system Am Heart J 29 526, 1945.
[9] Barnes, A R, and Whitten, M B Study of the R-T interval in myocardial infarction Am Heart J 5 142, 1929-30
[10] Gross, L The Blood Supply of the Heart New York, Paul B Hoeber, 1921
[11] Schlesinger, M J Significant Variations in the Anatomic Pattern of the Coronary Vessels, Blood, Heart and Circulation American Association for the Advancement of Science, Washington, 1940

CHAPTER IV

Physiologic Principles of the Circulation

THE FUNCTION of the circulation is twofold One is to collect and carry the nutritive products of digestion, the inhaled oxygen from the lungs, and the various endocrine products from the glands and tissues of their formation to all the cells of the body. The other is to collect the waste products of metabolism from all the tissue cells for excretion. Of the latter, the gaseous products, mainly CO_2, are carried to the lungs for their elimination and the others principally to the kidneys.

To prepare the products of digestion for utilization, to store some of the products and to eliminate the toxic elements, there is the interposition of the liver between the digestive tract and the systemic circulation The portal system of capillaries and veins form the circulatory link here, as described in Chapter III.

The capillary system is the primary functional portion, inasmuch as it is in direct contact with all the tissues of the body and carries on the interchange of materials between the tissues and the circulation. The rest of the cardiovascular system serves to maintain an adequate and proper capillary flow.

We shall attempt to discuss first the mechanism of distribution of the blood from the heart to the capillaries, then the capillary circulation with its interchange of materials between the blood and tissues and finally the return of the blood to the heart.

The subject will be discussed very briefly and in as simple a form as is possible to make it understandable for the application to clinical medicine For a more detailed and technical study, the reader is referred to standard textbooks on physiology, such as, Starling's, Wigger's, Macleod's and others, as well as to the innumerable excellent monographs and articles on the subject, only a few of which are quoted here

THE DISTRIBUTING SYSTEM

The most important part of the distributing system is the heart, which is the pump that sets the column of blood in motion Next in importance *are the elastic distention and rebound* of the central arteries and the contractile power of the smaller arteries and arterioles These will be discussed in order

Action of the Heart.

The blood, entering the auricles from the great veins, empties into the ventricles during the diastolic period of the latter. The first part of the

blood flow from the auricles to the ventricles, comprising about two-thirds of its volume, occurs by mere gravitational force. The last part, or the remaining one third, is propelled forward by auricular contraction. The main propelling force which carries the blood through the arterial system is exerted by the ventricular contraction.

The auricular contraction occurs in a peristaltic manner, starting normally in the right auricle at the mouths of the venae cavae, moving downwards to the ventricles According to Keith, regurgitation of blood into the great veins is prevented by the contraction of the taenia terminalis which is a broad band of muscle over the roof of the auricles. The duration of auricular systole is about 0 10 to 0 12 of a second It corresponds approximately to the duration of the P wave in the electrocardiogram

The ventricular systole is a composite of the fractionate contractions of the muscle fibers composing the various layers of the heart muscle As a result of contraction and shortening of all the muscle layers, as described in the third chapter, the size of the heart is greatly diminished in all diameters The base moves downward toward the apex and there is some rotation of the heart toward the right, bringing a portion of the left ventricular surface, especially the apex, toward the front and producing what is known as the apex beat

For a very brief period in early ventricular systole, before contraction has reached its peak, the intraventricular pressure is of sufficient degree to close the auriculo-ventricular valves but not high enough to open the semilunar valves, which are kept closed by the greater arterial pressure existing at the moment This is known as the period of isometric contraction Soon the intraventricular pressure becomes greater than the pressure in the aorta and pulmonary artery and the semilunar valves open, resulting in a sudden ejection of blood into the arterial tree The maximum ejection occurs in the early part of this phase and it becomes less as systole proceeds. The duration of the mechanical ventricular systole with a heart rate of 75 beats per minute is about 0 28 of a second, 0 05 of a second consisting of the isometric phase With faster heart rates, systole is very slightly shorter and with slower rates, very slightly longer The mechanical ventricular systole is very slightly shorter than the electrical systole. Its length may be approximately determined from the interval between the early part of the R wave to the end of the T wave in the electrocardiogram

The duration of ventricular diastole varies directly with the heart rate It may be calculated fairly accurately from the electrocardiogram, by measuring the distance between the end of the T wave and the very beginning of the QRS complex With a rate of 75 per minute, its duration is about 0.53 of a second In the first part, for a brief period of about 0 04 of a second, immediately after the termination of systole, the ventricular

chambers are again closed, for the auriculo-ventricular valves have not as yet opened and the semilunar valves have already closed. With greater relaxation of the ventricles, the auriculo-ventricular valves open and the flow from the auricles into the ventricles begins and continues throughout the rest of the diastolic period. The time relationship of the various events in the cardiac cycle, the heart sounds and the electrocardiogram are shown in Figure 25.

The volume of blood ejected by the heart, in man, in a given time, has been the subject of much investigation. Using the ethyl iodide method of Starr and Gamble,[1] the acetylene method of Grollman[2] and the simpler gasometric method recently described by Donal,[3] it has been variously estimated by different authors to be between 2.12 and 4.25 liters per minute

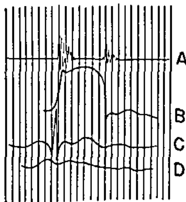


FIG 25.—TIME RELATIONSHIP OF THE VARIOUS EVENTS IN THE CARDIAC CYCLE. A, heart sounds, B, intraventricular pressure curve, C, electrocardiogram, and D, intra-auricular pressure curve.

in normal individuals. Variations in size and weight of the person determine to a great extent the volume output. Certain conditions such as the ingestion of food, the performance of exercise and hyperthermia increase the output greatly.

The stroke volume may be determined by dividing the minute volume output by the number of heart beats per minute. Its estimated amount, therefore, also varies in different cases and under different conditions. According to Grollman, the average is about 62 cc.

The normal optimal ventricular muscle contraction depends upon a given *stretch caused by the volume of blood entering the heart from the veins.* According to Starling,[4] the larger the volume of the heart, within normal physiologic limits, the greater the energy of its contraction and the amount of chemical changes at each contraction. Physical activity, by its muscular contraction, increases the venous return to the heart, as will be shown

later, and thus augments the heart volume Wiggers and Katz[5] have demonstrated that under normal conditions, the augmentation of the venous return on physical activity increases the velocity of ejection and prolongs systole As a result, there is an increase in both the stroke and minute volume output of the heart under such conditions, accelerating the rate of flow of blood to the active muscles and tissues

Another element that helps to increase the minute volume output of the heart under conditions of activity is reflex acceleration of the heart beat This is true, however, only if the acceleration of the heart is not excessive or far above the normal physiologic limits A great increase in the rate above normal will shorten the diastolic period thus diminishing ventricular filling and therefore the stroke volume As a consequence, the minute volume will diminish, inasmuch as the increased number of beats per minute may not compensate for the diminished stroke volume

Mechanism of Arterial Blood Flow

The arterial tree is never empty Even at the end of diastole the blood is moving forward under considerable pressure imparted to it by the previous ventricular systole, known as the diastolic pressure. When a new volume of blood is thrown into the aorta and pulmonary artery by systolic contraction of the ventricles, the pressure in the aorta and pulmonary artery is markedly increased This increase is known as the systolic pressure. The greatest increase occurs in the early part and reaches its maximum at about the middle of systole This maximum point is what we consider the systolic pressure, as determined by the sphygmomanometer The sudden increase in pressure produces distention or stretching of the aorta and pulmonary artery and imparts to their walls a considerable amount of potential energy The elastic rebound of the aortic and pulmonic walls converts this energy into kinetic energy used to move forward the volume of blood during the diastolic period

It will be seen that the aorta has the double function of storing some blood during the systolic period and of helping to propel it during the diastolic period Its storage capacity is about one-half of the blood discharged during systole, which is carried off during diastole This storage capacity is dependent upon the elastic property of the aorta which has its maximum expansibility and rebound in early life According to Hallock and Benson,[6] there is a progressive loss of the elastic quality of the aorta as age progresses, even in normal individuals Because of a compensatory increase in the dilatation of the aorta after 40 years of age, it assumes the role of a capacity chamber or reservoir, receiving the cardiac output without imposing undue strain on the heart

The pressure imparted to the blood in the aorta by the force of the

systolic contraction of the left ventricle results in a progressive compression of the column of blood from the aorta down to all its branches and their subdivisions. This causes the development of a wave of expansion, which may be felt over all the peripheral arteries as the pulse This wave travels faster than the actual movement of blood. Before ventricular systole is completed, it reaches as far as the leg vessels. This successive expansion of all the arteries down to the arterioles helps storing a considerable amount of the systolic discharge of blood from the heart in all the vessels. The contractile power of the muscular arteries promotes the flow of this stored blood during the diastolic period. There is thus a wonderful adaptation of the distributing system to any variations in the volume of circulating blood that may exist.

The actual velocity of blood flow is slower than the pulse wave Its speed also diminishes with increase in the subdivisions of arteries into arterioles and capillaries. This is due to the fact that the sum total of the cross sectional diameters of the smaller arterial branches of the arterioles and of the capillaries becomes progressively greater than the cross sectional diameter of the aorta. The greatest difference in the cross sectional diameter exists between the aorta and the capillary tree The average cross sectional diameter of the aorta is 3 centimeters The total cross sectional area of the capillary tree throughout the body has been estimated at about 500 to 800 times that of the aorta • Inasmuch as the average velocity of blood flow in the aorta is about 20 centimeters per second, the velocity of the blood flow in the capillaries would be 3/500 to 3/800 of 20 centimeters or approximately 75 to 1 2 of a millimeter per second The velocity of flow in the various medium sized arteries varies between 6 and 14 centimeters per second

The greatest velocity of flow occurs in the center of any vessel Under certain conditions where a sudden unusual acceleration of flow occurs, the difference between velocity of the axial stream and that of the peripheral stream may become quite marked This may occur especially in areas of vascular constriction or valvular orifices and is responsible in some cases for murmurs or arterial hums, as will be described in Chapter IX

According to Shipley and co-workers,[7] the flow pattern of the various arteries of the body varies considerably in amplitude, timing, duration and rate of flow In some arteries, actual backward components have occasionally been observed

Function of the Arterioles

The narrow caliber of the arterioles diminishes the intermittency of the arterial pulse, so that by the time the blood reaches the capillaries, its flow is continuous Intermittency of pulsation in the capillaries, however, may

occur in certain abnormal conditions where there is widespread dilatation of the arterioles The condition is then spoken of as "capillary pulsation," to be discussed in a later chapter.

By constant changes of the calibers of the arterioles, caused by dilatation and contraction of the circularly disposed muscular fibers, the flow to the capillaries is increased or diminished according to the need of various parts of the body If any tissue undergoes activity, the arterioles supplying that tissue dilate and thus flush the capillary vessels in that area In less active areas, the arterioles contract and diminish the flow of blood to those areas These vessels thus act as stopcocks between the arteries and capillaries. Their dilatation and constriction are independent of the expansion and contraction of the larger caliber arteries which are caused by general intra-arterial pressure

Arteriolar dilatation and constriction play a major role in maintaining normal blood pressure with its periodic fluctuations In conditions of abnormal widespread arteriolar constriction, arterial hypertension occurs.

The function of the arterioles then is to change an intermittent to a constant flow of blood, to regulate the local flow of blood to the capillaries, according to need, and to help maintain normal blood pressure with its periodic fluctuations An abnormal widespread arteriolar constriction results in arterial hypertension

Function of the Capillaries

The function of the capillaries may be fully appreciated only when we realize how extensive a ramification they form throughout the body and how closely they are in contact with all tissue cells The work of Krogh,[8] who made studies on capillary length, surface and volume in various organs gives us some conception of the extent of the capillary system.

Krogh estimated that in the entire muscular system of the average sized person, the total length of capillaries, if we were able to put them end to end, would perhaps stretch for a distance of 100,000 kilometers or about two and one-half times around the globe The total surface would be about 6,300 square meters. If all the capillaries of the musculature of the body would dilate to an average width of 8 micra, the skeletal muscle alone could hold 5 liters of blood, or more than the total estimated blood volume of an adult weighing 70 kilograms. This is based on the assumption that the estimated blood volume of a normal adult is about 75 cc per kilogram of body weight Actually, the exact blood volume in man has not been definitely established Various authors, using different methods of investigation, put it at 63 to 100 cc. per kilogram of body weight

The extensive length of the total capillary bed offers a tremendous surface for interchange of materials between the tissues and the blood. It is

estimated by Krogh that one cubic centimeter of blood comes in contact with 5,000 to 7,000 square centimeters of capillary surface.

The average length of a capillary is about one-half millimeter and its diameter varies between 3 and 20 μ in different regions, according to the state of dilatation. Each cell of the body comes in direct or in close contact with one or more capillaries, depending upon the functional importance of that cell.

The capillary blood supply to different tissues depends upon the activity of the given tissue at any moment. When a tissue is in a resting state, only $\frac{1}{20}$ to $\frac{1}{10}$ of the total capillary bed in that tissue is open to the circulation. The rest of the capillaries are emptied by the local constriction of the terminal arterioles or metarterioles and the capillaries themselves The metarterioles exhibit periodic dilatation and constriction at intervals of 15 seconds to 3 minutes, so that various portions of the capillary tree are flooded at different intervals. When a tissue becomes active, more of the metarterioles dilate, a greater number of capillaries open and the diameter of each capillary becomes wider. The extent of such increase in the capillary bed is in direct proportion to the amount of activity. Thus, in the resting muscle of a guinea pig, Krogh found that the number of open capillaries per square millimeter of muscle varied between 31 and 270, the diameter of the capillary, 3 to 3 8 μ and the capillary surface 3 to 32 square centimeters per 1 cc of muscle. At work, the number of open capillaries varied between 2,500 and 3,000 per square millimeter of muscle, the diameters of a capillary, 5 to 8 μ and the capillary surface 390 to 750 square centimeters per 1 cc of muscle, depending upon the degree of activity Krogh believes that the capillaries have tonus of their own and undergo contraction and relaxation independent of the corresponding arteriolar reaction This is the opinion also of nearly all other workers in the field.

The mechanism of capillary contraction and dilatation is still not entirely clear. It is believed, although not proven, that the Rouget cells in the capillary wall are the contractile elements

The capillary endothelium has great filterability. Under normal conditions, all crystaloids, gases and water pass through it very easily, in both directions. A small amount of the colloids likewise, may pass However, it is not permeable to the form elements of the blood

According to Landis,[9] the extent of capillary permeability and filterability is such that the estimated 6,300 square meters of capillary surface in the muscles of the body could filter the total plasma volume of man in 10 seconds, if there was no retaining force of fluid within the capillaries, and if the entire peripheral vascular bed would open simultaneously. The estimated average plasma volume in man is 49 per cent of the blood volume.

The movement of fluid, between blood and tissues, occurs in both directions, the rate and direction varying from time to time, according to the needs of the tissues During muscular activity more oxygen and fluid with its dissolved materials leave the blood than in the resting state. Also more CO_2 and fluid with waste products of metabolism re-enter the blood

Interchange of Material Between the Blood and Tissues According to Starling's theory,[10] which is widely accepted, the capillary endothelium is permeable to water and its solvents but relatively impermeable to colloidal plasma proteins The osmotic pressure of blood plasma, which is equivalent to approximately 7 times the atmospheric pressure, is due mainly to the crystaloids, gases and other easily transmissible substances. These are kept in a state of balance with similar substances in the tissue fluids and under ordinary circumstances do not influence the movement of fluid On the other hand, the colloidal plasma proteins, although exerting a much smaller osmotic pressure, estimated to be only about 25 to 30 millimeters of mercury, has a great effect on the movement of fluid, because they are relatively impermeable to the capillary endothelium

The movement of fluids and their solvents from the capillaries into the tissue spaces is accomplished by capillary blood pressure, variously estimated at 13 to 35 millimeters of mercury, which is always greater than the tissue pressure This movement will occur, however, only if the capillary pressure is greater than the colloidal osmotic pressure If the colloidal osmotic pressure is greater, the flow of fluid will be in the opposite direction, namely from the tissues into the capillary

Under normal conditions, the capillary pressure is greater than the colloidal osmotic pressure on the arteriolar end of the capillary and less on the venular end Hence, movements of fluids and their solvents will be in the direction from the capillaries into the tissues on the arteriolar side and back from the tissues to the capillaries on the venular side

This theory asumes, however, that the interchange of materials between the capillaries and tissues is based on purely mechanical factors Inasmuch as the capillary endothelium is not an inert membrane but consists of living cells, some of the processes of interchange of materials are undoubtedly due also to selective activity or biologic factors, besides the factor of osmosis Thus, by injecting dialized india ink into the blood stream, Krogh has observed its retention within the capillaries Being easily filterable, it should by the law of osmosis, leave the capillaries

The lower gradient of capillary pressure from the arteriolar to the venular end is not always constant. It is modified from time to time by changes in the caliber of arterioles Local arteriolar constriction will reduce the capillary blood pressure on the arteriolar end of the capillaries to a lower degree than on its venous end. Increased venous pressure may produce

similar results The dependence of the capillary blood pressure on the *local arteriolar inflow and venular outflow* is so marked that a given network of capillaries may at one moment be far above and at another far below the colloidal osmotic pressure, thus favoring massive filtration and massive reabsorption over large areas Alteration in posture and change in temperature may produce such effects.

Filtration or reabsorption of highly diffusible solutes to which the capillary wall is permeable does not necessarily follow the current of water Thus intravenous injection of a hypertonic saline solution will result in diffusion of some of the salt through the capillary wall toward the tissue spaces while fluid is moving from the tissue spaces towards the blood This continues until equalization of the electrolyte concentration occurs between the blood and tissue fluids. Capillary filtration is probably influenced to some extent by tissue pressure, resulting from the elastic rebound of the *connective tissues when distended by the fluids The studies of* Wells and co-workers[11] reveal that the pressure in various tissues varies normally between 2 and 12 centimeters of H_2O. In the presence of edema, it may rise to 26 centimeters.

Lymphatic Circulation and Capillary Filtration Much of the capillary filtrates of water, salts and the small amounts of proteins which enter the tissue spaces ultimately find their way into the lymphatic system which empties into the venous system. Drinker and Field[12] believe that the tissue cells or lymphatics may also produce some proteins which enter the lymphatic system, in addition to the small amount of the proteins derived from the capillary filtrate. The lymphatic vessels also drain off whatever particulate matter is found in the tissue spaces

Any interference with proper lymphatic drainage will have an effect on capillary filtration and tissue stagnation It plays a part in the pathogenesis of edema

Abnormal Factors Influencing Capillary Filtration: Capillary filtration is normally probably influenced by the state of innervation of the capillaries, by hormones, calcium and by temperature changes. Anrep[13] also observed that vasodilator substances of a histamine-like nature are produced and released by contracting muscle. Deficiency of O_2 and accumulation of CO_2 produce the same circulatory effects. Hemingway and McDowell[14] found that H ion concentration of the blood of 7.4 to 7.3 is also essential to the maintenance of normal capillary tone Concentration below 7 3 produces dilatation of the capillaries and increase in their permeability

It is thus seen that many factors may influence capillary dilatation. If these factors are of marked degree, they may produce injury to the capillary

wall and increase in its permeability An abnormal escape of the plasma proteins will then ensue, disturbing the balance between the colloidal osmotic pressure of the blood and the capillary blood pressure and thus predispose to edema Local application of excessive heat and cold, mechanical, chemical and toxic factors may also produce similar capillary wall injury, resulting in the same effects.

The Return of the Blood to the Heart

The blood leaving the capillary tree enters the venules and continues through the small veins and large veins, ultimately reaching the inferior and superior venae cavae and the right auricle

The force necessary to propel this blood upwards against gravity is greater than that produced by the pressure remaining in the column of blood after it traversed the capillary tree In other words, the pressure imparted to the arterial blood by the heart and the aorta is expended mainly in propelling the blood forward through the arteries, arterioles and capillaries *Comparatively little pressure is left beyond the capillaries, perhaps much* less than 30 millimeters of Hg This amount of pressure is not enough to raise a column of blood as far as the heart against gravity Other factors, therefore, must come into play to propel the blood toward the heart.

The most important factor, according to Henderson,[15] is the venopressor mechanism induced by tonic muscular contraction The entire musculature of a healthy man, even at rest, is exerting innumerable elastic pulls due to afferent and efferent nervous impulses These are much more marked during muscular activity These contractions and relaxations help fill the capillaries from the arterial side and empty them towards the venous side, thus acting as a "peripheral pump" or "booster," aiding venous return The extravascular support of the resisting elastic tissues of the body may also play a part

Other factors that help the movement of the venous blood forward are the suction effect of the thoracic cavity where the pressure is subatmospheric, the reduction of the pressure in the venae cavae by the continuous pumping effect of the heart and, the possible contraction of venules and veins in many parts of the body

Although the total amount of blood in the body is much less than that required to meet the metabolic needs of all tissues, if they were all active at once, under normal conditions the amount would be adequate. The reason is that only portions of the body tissues are active at any given time In fact, a considerable amount of available blood is not being used from time to time and is stored in various reservoirs of the body. Of these, the skin, the spleen and the splanchnic area comprise the main reservoirs for the right heart, and the lungs for the left heart. The much greater

capacity of the venous than of the arterial channels of the body an slower motion of blood in the former, makes the venous system part c reservoirs also.

During great muscular activity the blood from the various reservo emptied into the venous system and the massaging action of muscular tractions expedites its movements towards the heart. Backward m ment is prevented by the venous valves There is thus a constant r tribution of blood from less to more active tissues.

The Pulmonary Circulation

The venous blood leaves the right ventricle and flows through the *monary arteries, arterioles and capillaries In the latter, it is spread* over a tremendous surface in contact with the alveolar wall where oxygenated The oxygenated blood is then continued in its forward through the pulmonary venules, veins and finally reaches the main monary veins which empty into the left auricle

The amount of blood in the pulmonary vascular circuit, as determ by perfusion experiments in the dog by Daly,[16] is probably only abo per cent of the total volume of blood in the body

Because of the much shorter route and the lesser resistance of the flo blood in the pulmonic than in the systemic circuit, the work done by right ventricle, under normal conditions, is much less than by the l The muscle thickness of the former chamber is therefore much less t that of the latter, as shown in the previous chapter. The pulmonary ar and its subdivisions are likewise thinner and less elastic than the aorta *its branches. Under normal conditions, the pulmonary artery is there* less expansile and its rebounding force is smaller, so that the pulmon arterial pulse is transmitted with greater velocity than the systemic arte pulse.

The pulmonary arterial pressure is much lower than the systemic arte pressure Its estimated range varies between 22 to 60 systolic and 7 21 diastolic, with an average perhaps of 35 systolic and 15 diastolic gradient of pressure between the arteries and veins is perhaps 25 to The pulmonary capillary pressure is correspondingly lower than systemic capillary pressure It does not exceed normally, the onc pressure of the blood colloids, for if it did, exudation of fluid would t place into the alveolar spaces There is a considerable drop in pulmon vascular pressure during inspiration and rise during expiration due variations in the resistance to the flow of blood through the pulmon vessels during respiration.

Pulmonary arterial pressure may undergo periodic changes, independ of the amount of blood entering the pulmonic circuit. Such changes

due to variations in the peripheral resistance of the pulmonary arterioles Increased output of the right ventricle, due to greater systemic venous inflow also increases the pulmonary arterial pressure.

The flow of blood through the pulmonary arterioles and capillaries was found to be inconstant by Wearn and co-workers [17] It changes spontaneously as well as under the effect of drugs. The number of capillaries through which blood flows at a given time varies greatly and may represent a small fraction of the total number of capillaries in the lungs. More of the capillary bed comes into activity when greater aeration of blood is necessary under physical effort and strain.

The bronchial arteries supplying blood to the bronchial tree and pulmonary tissues do not have any extensive arterial and venous communications with the pulmonary vascular supply, according to Berry and co-workers [18] The main communications exist between the capillaries of the two systems, although some of the small arterioles may also intercommunicate

Nervous and Chemical Regulation of the Circulation

The normal coordination of the circulation to meet the metabolic needs of the various tissues of the body is maintained by a specialized portion of the nervous system In recent years it has been demonstrated that the mode of action of the nervous elements is probably through their production of chemical substances Thus, the vasoconstrictor nerves produce their effects through the liberation of adrenergic substances or sympathin and the parasympathetics through the liberation of cholinergic substances The activities of the nervous mechanism are also greatly modified by chemicals and hormones elaborated in other parts of the body, such as pituitrin, histamine, acetylcholine, adrenalin and thyroxin.

The specialized nervous system regulating the circulation consists of the cardioaccelerator and inhibitory nerves controlling the heart, and the vasoconstrictors and dilators controlling the arterioles, capillaries and probably also the venules and small veins A diagrammatic representation of the nervous control of the circulation is shown in Figure 26.

The *cardioaccelerator* nerve fibers originate in nerve cells or centers located in the five upper dorsal segments of the cord They pass through the stellate and upper dorsal sympathetic ganglia as white rami and thence they continue to the heart in a complex plexus of fibers It is assumed, but not yet fully established, that a controlling cardioaccelerator center is present also in the floor of the fourth ventricle of the brain

The *cardioinhibitory* center is located in the vagal nucleus in the medulla.

The *vasoconstrictor* center is located in the region of the facial nucleus at the floor of the fourth ventricle. Nerve fibers originating from the cells in this area descend in the anterolateral tract of the cord and terminate at

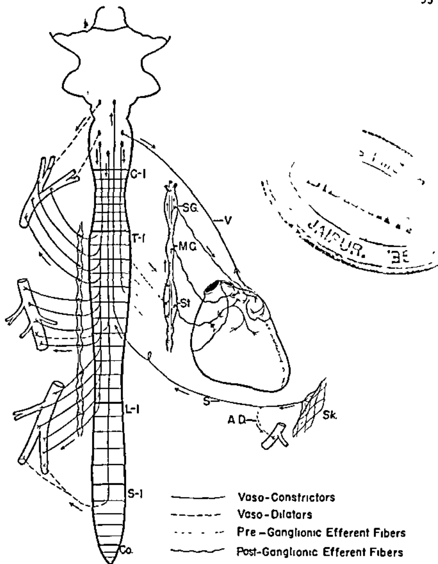


FIG. 26.—DIAGRAMMATIC REPRESENTATION OF THE NERVOUS CONTROL OF THE CIRCULA-

right, originating from the skin, Sk, in the sensory nerve, S

various levels, making synaptic connections with nerve cells located in regions of the cord between the first thoracic and first lumbar areas. Fibers of the latter nerve cells course through the sympathetic system, supplying

the various vascular areas of the body. The splanchnic nerves carry the greatest number of these and are the most important vasoconstrictors in the body. The spinal centers are thus coordinated and dominated by the higher medullary center.

Vasodilator fibers originate from neurons in various parts of the central nervous system. Many of these emerge in the parasympathetic outflow in the seventh, ninth and tenth cranial nerves and in the sacral outflow. A few pass through the sympathetic nerves to the blood vessels of the heart Some vasodilator impulses appear to be carried to the peripheral vessels by the sensory nerves Inasmuch as the sensory nerves transmit only afferent impulses, the vasodilator reaction by these nerves is therefore spoken of as antidromic They are carried by branches of sensory nerve fibers which split off and supply local blood vessels. There appears to be a tonically active vasodilator center in the medulla which has some controlling effect on the vasodilation

Although the medullary centers have controlling and coordinating effects on the spinal centers, they themselves are modified by higher centers in the brain located in the hypothalamic and cortical areas. Thus, fear, excitement, and other mental activity may result in cardioacceleration, increased amplitude of cardiac contraction and widespread vasoconstriction, causing a rise in blood pressure In some cases, mental and emotional disturbances may produce marked slowing of the heart and vasodilation with drop in pressure, resulting in fainting Also skin reactions such as pallor and flushing are examples of local vascular response to psychic activity

The various centers are also activated reflexly by impulses originating in pressor receptor innervations in various vascular areas of the body. Thus, slowing of the heart and a drop in blood pressure may result from stimulation of the carotid sinus and the aortic regions by an increase in the intra-aortic and intra-carotid pressure.[19, 20] It may also result from chemical stimulation of the carotid bodies Similar effects have been attributed to impulses originating in the superior and inferior venae cavae, right auricle, and pulmonary veins Thus, Daly and co-workers[21] have observed a slight fall of the systemic blood pressure and a rise or fall in the heart rate, when the pulmonary blood flow was increased. Section of both cervical sympathetic nerves abolishes such effects In some instances an increase in pulmonary flow also causes acceleration of respiration

Vascular changes have also been observed by Gammon and Bronk,[22] as a result of impulses discharged from the pacinian corpuscles in the mesentery which lie close to the mesenteric vessels.

Somatic nerve stimulation may also produce reflex vasoconstriction or dilation and cardioinhibition or acceleration. Thus, application of heat may result in a fall in blood pressure and changes in heart rate. Cold will

produce elevation in blood pressure Manipulation of some of the abdominal viscera may result in cardioinhibition and a drop in pressure

Marked anoxia and increase in CO_2 may react in various ways on different parts of the reflex arcs Acceleration or slowing of the heart may occur. Locally they may produce vasodilation Their action on the vasomotor center, however, may result in widespread vasoconstriction and rise in blood pressure.

Under normal conditions, even without undue stimulation, the various nerve elements are more or less tonically active This tonic activity is the result of impulses continually flowing in and out of the centers The heart rate is thus maintained at a normal level by the tonic activity of the accelerator and inhibitory nerves which counterbalance each other Vasoconstriction is maintained at a normal level by the tonic activity of the *vasoconstrictor center* Because the various centers are widely scattered in the cord and the brain stem, the discharge of impulses may be massive and widespread or fragmentary and localized to given sections of the body as per requirement Widespread discharge originates from the higher centers while local discharge originates in the cord

It is interesting to find, as was beautifully demonstrated by Cannon and co-workers,[23] that complete bilateral sympathectomy does not prevent the animal from performing its normal functions They observed that the sympathetico-adrenal system is of great service in critical emergencies but is not indispensable under normal conditions

REFERENCES

1 Starr, I, Jr, and Gamble, C J An improved method for determination of cardiac output by means of ethyl iodide Am J Physiol 87 450, 1928
2 *Grollman, A A comparison of the triple extrapolation (Fick principle) and the acetylene* (foreign gas principle) methods for the determination of the cardiac output in man Am J Physiol 93 116, 1930
3 Donal, J S A convenient method for the determination of the approximate cardiac output in man J Clin Investigation 16 879, 1937
4 Starling, E H The Linacre Lecture on the Law of the Heart London, 1918
5 Wiggers, C, and Katz, L The contour of the ventricular volume curves under different conditions Am J Physiol 58 439, 1922
6 *Hallock, P, and Benson, I C Studies on the elastic properties of human isolated aorta* J Clin Investigation 16 595, 1937
7 Shipley, R E, Gregg, D E, and Schroeder, E F An experimental study of flow patterns in various peripheral arteries Am J Physiol 138 718, 1943
8 Krogh, A Anatomy and Physiology of the Capillaries, ed 2 New Haven, Yale University Press, 1929
9 Landis, E M Capillary pressure and capillary permeability Physiol Rev. 14 404, 1934
10 Starling, E H. The Fluids of the Body Chicago, Chicago Medical Book Co, 1909
11 *Wells, H S, Youmans, H S, and Miller, D G, Jr* Tissue pressure (intracutaneous, subcutaneous and intramuscular) as related to venous pressure, capillary filtration and other factors J. Clin Investigation 17 489, 1938.

[12] Drinker, C. K, and Field, M E Lymphatics, Lymph and Tissue Fluids Baltimore, Williams & Wilkins, 1933
[13] Anrep, G. V Studies in Cardiovascular Regulation Lane Medical Lectures, Stamford University Press, 1936.
[14] Hemingway, A, and McDowall, R J S The chemical regulation of capillary tone J. Physiol. 62 166, 1926
[15] Henderson, Y Tonus and the venopressor mechanism The clinical physiology of a major mode of death Medicine 22 223, 1943
[16] Daly, D I Observations on the blood-perfused lungs of the dog, guinea-pig and Macacus rhesus with special reference to spontaneous lung movements Quart J Exper Physiol 28 357, 1938
[17] Wearn, J T, Ernstene, A C, Bromer, A W, Barr, J S, German, W. J, and Zschiensche, L. J The normal behavior of the pulmonary blood vessels with observations on the intermittence of the flow of blood in the arterioles and capillaries Am J Physiol 109 236, 1934
[18] Berry, J L, Brailsford, J F, and Daly, D I The bronchial vascular system in the dog Proc Roy Soc, London, s B 109 214, 1931
[19] Sigler, L H Hyperactive cardioinhibitory carotid sinus reflex Arch Int Med 67 177, 1941
[20] —— Hyperactive vasodepressor carotid sinus reflex Arch. Int. Med 70 983, 1942.
[21] Daly, D I, Lundany, G, Todd, A, and Verney, E B Sensory receptors in the pulmonary vascular bed Quart J Exp Phys 27 123, 1937
[22] Gammon, G D, and Bronk, D W The discharge of impulses from pacinian corpuscles in the mesentery and its relation to vascular changes Am J Physiol 114 77, 1935
[23] Cannon, W B, Newton, H F, Bright, V M, and Morre, R M Some aspects of the physiology of animals surviving complete exclusion of sympathetic nerve impulses Am J Physiol 89 84, 1929

CHAPTER V

The Normal Sized Heart and its Measurements

THE SIZE of the heart and its position in the chest cavity may be determined fairly accurately by physical examination and by roentgenologic study The former has the advantages of being always available to those who acquire the skill. The latter has the advantage of being more accurate and in enabling us to visualize the heart in more than one view.

The size and appearance of the normal heart, as determined by these methods, vary considerably in different individuals and at different ages. Normalcy, therefore, is relative. What is normal for one person may be abnormal for another Furthermore, even if the heart is of normal size *and shape for the given individual, it may be the seat of considerable disease* and may thus give us a wrong impression in diagnosis. It is a very serious mistake, therefore, to rely only on the appearance and size of the heart for the diagnosis of heart disease in cases where the patient complains of disturbances referable to the cardiovascular system. If the heart is found to be enlarged or of abnormal shape, it will be of help in diagnosis. Even then, the actual diagnosis must depend upon its correlation with other signs and symptoms. If the heart is found to be of normal size and shape, the diagnosis will depend entirely upon other clinical and laboratory findings

Nevertheless, if for no other reason than the fact that a definitely enlarged heart and one which is grossly abnormal in configuration is always an abnormal heart, it is essential to know its normal limits.

Landmarks of the Chest

To determine the boundaries of the heart and great vessels, we employ the sternum, *ribs and certain imaginary lines as landmarks* The sternum and ribs are determined by palpation as follows: The *suprasternal or jugular notch* is felt as a depression on the top of the manubrium. This is on the same plane as the lower border of the second thoracic vertebra. The *sternal angle*, is felt as a prominent projection at the junction of the manubrium and body of the sternum. It is the location where the second costal cartilage on each side joins the sternum, and is on the same plane as the fifth thoracic vertebra. Beginning with the sternal angle, the various ribs and their interspaces can be easily counted The area where the body of the sternum joins the xyphoid is on the same plane as the cartilage between the ninth and tenth thoracic vertebrae.

The imaginary vertical lines on the surface of the chest employed as landmarks are the midsternal line, midclavicular lines and the axillary lines. The *midsternal line* runs vertically downward in the middle of the sternum. The two *midclavicular lines* run vertically downwards from the center of each clavicle The *anterior and posterior axillary lines* run vertically downwards from the respective axillary folds, and the *midaxillary lines* run vertically from the apex of each axilla Occasionally, we speak also of the *lateral sternal lines* along each sternal margin and the *parasternal lines* between the lateral sternal and midclavicular lines Such lines, however, are of no advantage

Surface Boundaries of the Heart and Great Vessels

In normal individuals, the apex of the heart is usually located in the fifth intercostal space, 8 to 9 centimeters from the midsternal line

A line drawn vertically downward on the right of the sternum, about 4 centimeters from the midsternal line, extending from the third to the fifth right costal cartilage and continued to the sternal end of the sixth right costal cartilage represents the right margin of the heart, formed by the right auricle. A line extending from the sixth right costal cartilage to the apex represents the inferior margin, formed by the right ventricle except for the extreme left end which is formed by the left ventricle.

A line drawn from the second left interspace close to the sternal margin, extending obliquely downwards to the apex with some convexity to the left, represents the left border of the heart, formed by the left ventricle. Another line drawn parallel to this and about a finger's breadth to the right, corresponds approximately to the location of the anterior longitudinal sulcus, between the right and left ventricles.

A line extending from the third left to the sixth right costo-sternal junction represents the approximate location of the coronary sulcus, between the right auricle and right ventricle The right auricle is above that line, the right ventricle below.

The pulmonary orifice is at a level of the upper angle of the third left costo-sternal junction. The aortic orifice is a little lower and closer to the midsternal line. The mitral orifice is to the left of the midsternal line opposite the fourth costal cartilage. The tricuspid orifice is somewhat lower and to the right These are the anatomic locations and not the areas where the maximum sounds and murmurs are heard, as will be described in Chapters VIII and IX

The superior vena cava extends in a straight line from the lower part of the first to the upper part of the third costal cartilage, close to the right side of the sternum.

The pulmonary artery extends from the second left interspace close to the sternum in an upwards and backward direction.

The ascending aorta commences at a level of the third left costal cartilage and the adjoining left half of the sternum and ends at a level of the upper border of the second right costal cartilage The arch extends from the

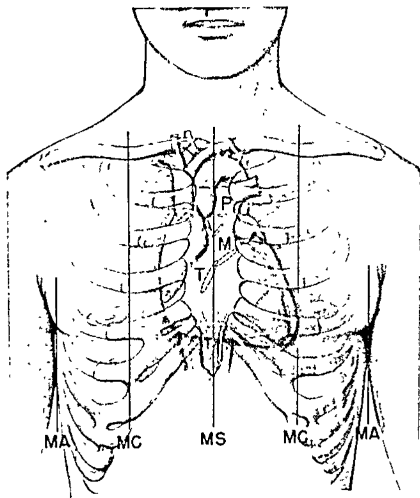


FIG. 27 —SURFACE BOUNDARIES OF THE HEART AND GREAT VESSELS, AND LOCATIONS OF THE VALVULAR ORIFICES AND IMAGINARY LINES Orifices. P, pulmonic; A, aortic, M, mitral, and T, tricuspid Imaginary lines MS, midsternal, MC, midclavicular; MA, midaxillary

latter location to a level of the fourth thoracic vertebra The descending thoracic portion extends from the fourth to the twelfth thoracic vertebra. Figure 27 shows the surface boundaries of the heart and great vessels as well as the locations of the sulci and valve orifices

Tracheo-bronchial and Esophageal Relations

The close relationship of the trachea, esophagus and the primary bronchi to the heart and aorta are often valuable in mapping out roentgenologically the enlargement of certain portions of the latter organs. It is essential, therefore, that we have in mind the normal relationship of these various organs in the thoracic cavity

The trachea extends from the level of the sixth cervical to the upper border of the fifth thoracic vertebra where it bifurcates at the lower level of the aortic arch into the two primary bronchi Its area of bifurcation is approximately at the level of the sternal angle. It is about eleven centimeters long and slightly over two centimeters wide At first, it is centrally placed, but it inclines slightly to the right as it enters the chest. Immediately above its bifurcation, it is in direct contact with the aortic arch, which lies anteriorly and winds around the left bronchus.

The *right bronchus* is in a more direct line with the trachea than the left It is about 2 5 centimeters long

The *left bronchus* is narrower and longer than the right It is of greater importance than the right bronchus for delineating the heart and aorta in disease, for it passes beneath the aortic arch and is not far removed from the left auricle Aneurysms of the arch in this location will displace the left bronchus and may produce the so-called "tracheal tug," to be described in Chapter XX Marked enlargement of the left auricle will displace the left bronchus upwards.

The esophagus extends from the sixth cervical to the eleventh thoracic vertebra, along the vertebral column, posterior to the trachea and the other organs and presents slight antero-posterior and lateral curvatures

In the cervical portion, it is situated in the midline. At the root of the neck, it inclines slightly to the left but is pushed to the midline again by the aortic arch and left bronchus It then deviates to the left down to the esophageal hiatus in the diaphragm.

The esophagus may be visualized roentgenologically by filling it with an opaque medium as barium sulphate, shown in Figures 28 to 35 When so visualized, it normally presents some indentations in the region of the aortic arch and the left bronchus and very slight deviations in the regions of the left auricle and descending aorta Greater indentations or displacement of the esophagus will help determine enlargement of these structures, as will be shown later.

Outlining the Heart by Physical Examination

Bearing in mind the normal anatomic boundaries, we may determine the size and shape of the heart with fair accuracy, in a good percentage of cases, by inspection, palpation and percussion. In many cases, however,

these methods fail to give us a clear outline because of the constitutional build of the individual or for other reasons, to be discussed shortly.

Inspection: As applied to the determination of the size of the heart, inspection consists of a careful visual examination of the precordial area for the maximal cardiac impulse which normally *designates the location* of the apex of the heart.

To visualize this area clearly, the front of the chest must be exposed to proper light, and the patient should be, if possible, in an upright position because in the recumbent, the apex may normally be displaced from its usual position

In some cases, the maximum apical impulse is localized to an area of about one centimeter diameter In others, it extends over an area several centimeters in diameter. Here, the area of the greatest excursion is the site of the apex In thin-chested individuals, there may be a slight heave over the entire lower precordium, due to right ventricular contraction *Here also the area of the maximum impulse designates the location of* the apex.

Although in the average normal individual the apex impulse is located within the midclavicular line, or 8 to 9 centimeters from the midsternal line, in the fifth left intercostal space, its location may vary considerably in individuals who deviate greatly from the average constitutional build Thus, in small, thin persons, it may be seen at a point only 6 centimeters from the midsternal line, while in long-chested individuals with oblong and verticle-shaped hearts, the apex impulse may extend down to the sixth interspace close to the sternum. In broad-chested individuals with very high diaphragms, it may be seen in the fourth interspace, ten centimeters from the midsternal line This may also occur when the diaphragm is raised by an increase in intra-abdominal pressure such as that caused by pregnancy, ascites, tumors and obesity.

Palpation This is another method of determining the point of the maximum cardiac impulse as well as its force, rate, and regularity It is a far more valuable method than inspection in determining the degree of displacement of the apex in the different recumbent postures, for the visual method cannot be properly applied when the patient is in the left lateral recumbent posture. Normally, the apical impulse, as determined by palpation, will shift as much as 5 centimeters or more when the patient is turned from the left to the right lateral recumbent position.

To palpate the apical impulse properly, the entire palm of the hand is placed over the left lower precordium, and the area of the impulse, if any is present, is determined. The point of maximum heave may then be palpated more specifically with the finger.

The apical impulse may be most easily determined by palpation in young individuals. As age progresses and with increase in thickness of the chest wall, its determination is at times difficult and occasionally impossible. In some such cases, this sign may be elicited best when the patient bends forward.

In most pathologic conditions, such as pulmonary emphysema, hydrothorax, pneumothorax and pericardial effusion, the apical impulse cannot be felt.

Increase in the area and amplitude of the cardiac impulse may occur in hyperaction of the heart induced by excitement, extreme strain, thyrotoxicosis, psychoneurosis and stimulating drugs.

Percussion: Percussion of the heart borders, if properly practiced, will help to determine not only the apical region but also the right and left borders of the heart and the basal vessels. It should always be used in addition to inspection and palpation and not as a substitute Very often we may get more information from one or the other method, but all methods combined will increase the chances of exact determination of the heart size

The methods employed in percussion are fully discussed in textbooks on physical diagnosis As applied to the heart, it is the author's practice in doubtful cases to percuss one intercostal space at a time, beginning with the second and going downward, first on the left, then on the right side of the chest. The pleximeter finger is placed in each space, about 3 centimeters from the expected location of the border of the heart and gradually moved towards the heart in short steps The author employs fairly heavy percussion for the average case, and lighter percussion in thin-chested individuals or in children The first point where dullness is heard is marked off in each intercostal space. A line drawn on each side and connecting these points should represent the borders of the heart. As a further check, percussion is repeated with the pleximeter finger parallel to that line, again starting about three centimeters away and gradually moving towards it. The area of dullness should fairly well correspond in both instances if percussion is properly performed and if the ear is well trained

Like other methods of diagnosis, percussion often fails to help outline the heart correctly. This is true especially in the presence of a thick chest, large breasts and pathology in the pleuro-pulmonary fields such as emphysema, pneumothorax, hydrothorax and so on In some cases, gaseous distention of the abdomen will modify the percussion sound and thus interfere with its proper evaluation

For practical purposes it is not necessary to measure the distance of the cardiovascular borders in each intercostal space. It is sufficient in most cases to measure the area of dullness extending from the midsternal line in the second and fourth intercostal spaces on the right and in the third and fifth or sixth interspaces on the left.

In normal individuals, no dullness is detectable in the second right interspace beyond the sternal border. Definitely detectable dullness extending in that interspace beyond the sternum speaks either for widening of the basal vessels or for the presence of superior mediastinal pathology. In the fourth right space, dullness should normally not extend more than 4.5 centimeters from the midsternal line in broad-chested individuals, or 3.5 centimeters in slim persons. In the third left interspace, dullness should normally not extend more than 4 centimeters from the midsternal line. In the apical region, dullness usually extends about 1 centimeter to the left of the maximum apical impulse as determined by inspection and palpation.

Outlining the Heart by Roentgenologic Methods

The size and shape of the heart and the vascular pedicle can best be determined by roentgenologic examination. By this method we can also visualize the individual heart chambers and the amplitude and regularity of their contraction.

The usual methods of roentgenologic examinations consist of fluoroscopy, orthodiagraphy and teleoroentgenography. Within recent years, other methods have been developed, such as roentgenkymography, angiocardiography and electrokymography. These methods, however, are rather complicated and are as yet not widely used.

Fluoroscopy. This method is the most easily performed. It consists of direct visual examination of the heart and the basal vessels in their relation to the thoracic wall and other thoracic structures.

The usual positions of the patient in which this examination is performed are the *antero-posterior*, *right anterior oblique*, *left anterior oblique* and occasionally also the *left or right lateral*. Enlargement of the individual chambers of the heart can often be determined only in one or the other of these positions.

The *antero-posterior view* is obtained by placing the patient's anterior chest wall against the screen, facing the examiner, the tube being behind the patient's back. The *right anterior oblique view* is obtained by placing the patient's right anterior portion of the chest against the screen at an angle of about 50 degrees, the tube being, therefore, behind the patient's left posterior part of the chest. The *left anterior oblique view* is obtained by placing the patient's left anterior portion of the chest against the screen at an angle of about 50 degrees, the tube being, therefore, behind the patient's right posterior part of the chest. The lateral views are obtained by placing either the right or left lateral sides of the chest against the screen, the tube being behind the opposite side.

It is advisable to inspect carefully the various parts of the heart and great vessels as well as the other thoracic structures and organs by slowly

rotating the chest from one position to the other. Some abnormalities may often be discovered in some in-between position.

Orthodiagraphy This is a graphic recording of the size and shape of the heart and great vessels as seen on the fluoroscopic screen Several methods are employed. The usual one consists of directing the central ray of a freely movable fluoroscopic tube on a stationary screen. The tube shutter is closed down to a degree which will permit only the passage of the central rays This is moved along the cardiovascular and chest borders, sketching the outlines of these borders with a pencil on the screen

Teleoroentgenography This consists of an x-ray film obtained with the patient at a great distance from the tube, so as to prevent too much divergence of the rays At a distance of about six or seven feet, the x-rays are more or less parallel, thus overcoming much of the distortion of the chest and its organs

Both, the orthodiagram and teleoroentgenogram can be obtained not only in the antero-posterior view but also in the other views mentioned under fluoroscopy The positions of the patient are the same

Advantages of the Three Methods Each of these three methods has its advantages and disadvantages. *Fluoroscopy* has the main disadvantage of being a visual method, and does not yield a permanent record. Another disadvantage is that ordinarily the tube is very close to the screen, resulting in some distortion of the heart and great vessels as well as the chest. It has its great advantages, however, in being simple to operate and in helping us to determine at a glance the general appearance of the heart and other thoracic structure With adequate experience, it is easy to determine normality or abnormality. In fact, because of a certain degree of magnification of the heart, we are able to visualize and delineate the borders of its chambers with greater ease We are also able to determine the size and shape of the heart and great vessels during systole and diastole and during the various phases of respiration With the teleoroentgenograms, we do not always know in which phase of the cardiac cycle the picture was obtained.

Orthodiagraphy has the advantage of producing a graphic record of the visual fields Because of the utilization of the central ray, the diameters of the heart and great vessels are of more correct natural proportions. The method, however, is time consuming and requires considerable experience. Also being a subjective method, the visual acumen of the examiner and his ability to record accurately what he sees, must be considered in evaluating any orthodiagram

The *teleoroentgenogram* has the advantage of being strictly objective and gives us, in addition, details of the lung fields and hilar markings Ac-

cording to Edeiken,[1] however, there is somewhat greater magnification of the heart and especially the aorta in a teleoroentgenogram than in the orthodiagram. The transverse diameter of the chest is relatively more magnified in a teleoroentgenogram than in an orthodiagram so that the relation of the heart to the chest is relatively smaller in the former than in the latter.

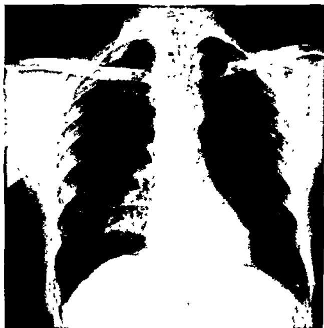


FIG 28 —ANTERO-POSTERIOR VIEW OF THE HEART AND VASCULAR PEDICLE IN TO THE TRACHEA, BRONCHI AND ESOPHAGUS

THE NORMAL BORDERS OF THE HEART AND VASCULAR PEDI

The heart silhouette, as seen by roentgenologic examination, appears as a single outline because the four chambers composing it are superimposed upon one another Only the outer walls of the chambers comprise the picture Inasmuch as no lines of separation of the chambers are evident roentgenologically, the outline of the entire heart appears single

From an anatomic knowledge, however, we can tell to which chambers the various sections of the silhouette belong Enlargement of a given chamber can thus be determined by an abnormal bulge of a given portion of the silhouette. For this reason, the examination must be done in the various positions, enumerated above. The normal outlines are as follows.

In the *antero-posterior position*, Figures 28 and 29, from above, down-

wards, the right border is made up of the superior vena cava and the right auricle, the last occupying approximately *one-half of the length of this* border. The lower part of the superior vena cava shadow merges with the aortic shadow but in most cases the right aortic border does not extend *beyond the border of the vena cava In vertically shaped hearts, the* inferior vena cava may occasionally be seen in the right cardio-hepatic angle, especially in inspiration

The left border is made up of the rounded outline of the aortic arch, the so-called knob, the pulmonary artery, the left ventricle, the last com-

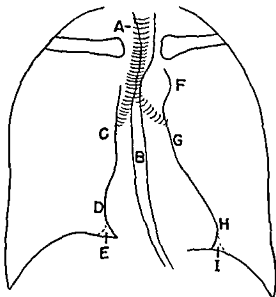


FIG 29 OUTLINE OF FIG 28 A, trachea and bronchi, B, esophagus, C, superior vena cava, D, right auricle, E, inferior vena cava, F, aortic knob, G, pulmonary artery, H, left ventricle, I, *epicardial fat*

prising approximately two-thirds of that border. In the left cardio-diaphragmatic angle, a triangular shadow of lesser density than that of the heart is often seen due to epicardial fat

The inferior border usually merges with the diaphragmatic shadow and cannot be made out.

In the *right anterior-oblique view*, Figures 30 and 31, the right border, that is on the operator's left, from above downwards, consists of the superior vena cava and right auricle. At the lowest part, the inferior vena cava may be seen, especially in longitudinally-shaped hearts The upper part of the superior vena cava is obscured by the trachea and bronchi The border, left that is on the operator's right, is made up of the aorta, the



FIG 30—RIGHT ANTERIOR OBLIQUE VIEW OF THE HEART AND VASCULAR PEDICLE

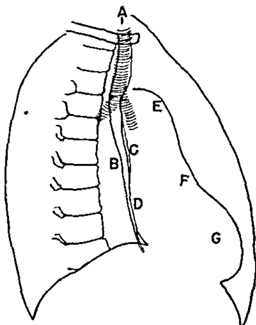


FIG 31—OUTLINE OF FIG. 30 A, trachea and bronchi; B, esophagus, C, superior vena cava, D, right auricle; E, aorta; F, pulmonary conus; G, right ventricle.

pulmonary conus and right ventricle from above downward. The descending aorta may be visualized in some cases between the posterior surface of the heart and spinal column

In the *left anterior oblique view*, Figures 32 and 33, the right border, that is on the operator's left, from above downwards, is the superior vena cava, the right auricular appendage and the right ventricle. The ascending portion of the aortic arch normally does not extend beyond the border of



FIG 32.—LEFT ANTERIOR OBLIQUE VIEW OF HEART AND VASCULAR PEDICLES.

the superior vena cava The visible part of the left border, that is on the operator's right, are the left auricle and ventricle An area of hyperillumination is observed between the region of the lower border of the aortic arch and the upper region of the pulmonary artery, known as the "aortic window" This is produced by the trachea and its bifurcation.

In the *left lateral position*, Figures 34 and 35, the anterior border, at the operator's left, from above downward, is made up of the superior vena cava, aorta, pulmonic conus and right ventricle The posterior borders, at the operator's right, are made up of the left auricle and ventricle. Between the heart and the sternum there is a clear triangular area, known as

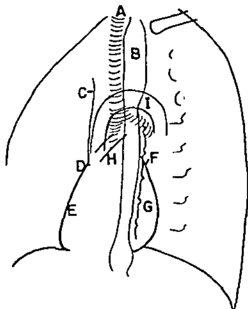


FIG. 33.—OUTLINE OF FIG. 32. A, trachea and bronchi, B, esophagus, C, superior vena cava, D, right auricular appendage, E, right ventricle, F, left auricle, G, left ventricle, H, pulmonary artery; I, aorta.



FIG. 34.—LEFT LATERAL VIEW OF HEART AND VASCULAR PEDICLE.

the retrosternal triangle. Normally, there is also a clear area between the posterior part of the heart and spine, spoken of as the retrocardiac clear space

Roentgenkymography This consists of a graphic x-ray recording of the heart contraction as shown by the movements of the cardiovascular borders As originally developed by Sabat,[2] in 1911, a single slit grid was used. The method ordinarily employed now, as developed by Stumpf,[3] in 1931, consists of a lead sheet with multiple equidistant parallel slits. The slits are 0 4 mm wide and the distance between them is 12 mm. The size of the

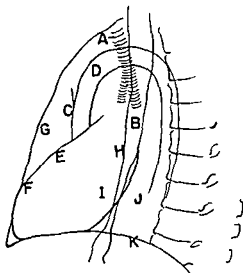
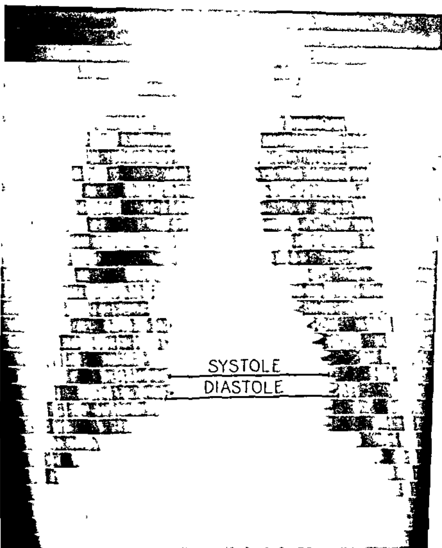


FIG 35 —OUTLINE OF FIG 34 A, trachea, B, esophagus, C, superior vena cava, D, aorta; E, pulmonic conus, F, right ventricle, G, retrosternal triangle, H, left auricle, I, left ventricle, J, retrocardiac clear space, K, right dome of the diaphragm

lead sheet is large enough to cover the entire cardiovascular area and it is placed between the casette holding the film and the patient. The casette is made to move slowly downward during an exposure of 1 to 2 seconds The movement is timed so that it includes as least one complete cardiac cycle, and the distance it travels is less than 12 millimeters to prevent overlapping of the x-ray shadows.

The picture obtained consists of multiple wavelike projections from the heart borders, as shown in Figure 36, which represent pulsations of the recorded areas *Depending upon the duration of the contraction and relaxation* of a given part of the cardiovascular region in relation to the slit, we get a corresponding projection or depression. Thus, if the movement of the heart in a given area is parallel to the slit, it will be recorded as a

wave. If it is at right angles or if there is no movement, it will be in the form of a straight edge.



IG 36—ROENTGENKYMOGRAM (Courtesy Dr. Richard Gubner) For description, see text.

The ventricular wave or projection represents diastolic filling, the peak epresenting the maximum diastole. The sharp inthrust represents systolic contraction, the trough being the maximum systole. The aortic expansion wave is synchronous with ventricular systole

§ The subject has been well covered by Gubner and co-workers[4] who consider this method of value in the diagnosis of myocardial infarction and other diseased states. Keys and associates[5] have utilized this method for estimating the volume output of the heart.

It must be realized, however, that the movements of the heart consist not only of contraction and relaxation of its walls but also of total displacement, tortion and rotation during systole and diastole, as described before and as was demonstrated by Wolferth and Margolies[6] These movements should necessarily add or subtract from the values of the waves as expressed by ordinary systole and diastole in different individuals, depending upon the shape and position of that organ. In interpreting the waves, consideration must, therefore, be given to these factors The method, nevertheless, may have value in diagnosis.

Angiocardiography This consists of visualization of the individual chambers of the heart and thoracic vascular tree by the injection of a radio-opaque solution such as 70 per cent diatrast into a principal vein in the arm and rapid x-ray exposures of the chest. The first successful result of this procedure was obtained by Robb and Steinberg.[7] They felt that the method was quite safe and practical and yielded a great deal of information of the normal heart and great vessels as well as of pathologic conditions It requires, however, special technic and teamwork, and cannot be used universally It should be employed in those diseased states where visualization of the individual chambers and various parts of thoracic vascular radicles is essential for differential diagnosis, such as congenital defects. The method is also of great value in differentiating tumors located close to the heart and main vessels from aneurysms

Electrokymography: This consists of recording by a galvanometer the movements of given portions of the heart and great vessels as seen fluoroscopically. A photosensitive pickup is used for transmitting these movements to the galvanometer The results are practically the same as those of roentgenkymography except that the study here is confined to local areas of the heart or vessels. The subject is fully described by Boone and co-workers.[8]

Measuring the Heart and Great Vessels

It is often necessary to determine the extent of cardiac enlargement and aortic widening. For this reason, we must know the measurements of the average normal heart.

The standard measure frequently employed in roentgenology is the so-called cardiothoracic ratio. It consists of determining the lengths of the transverse diameter of the heart and the internal transverse chest diameter,

and dividing the former by the latter figure. Thus, if the transverse diameter of the heart, as measured by the distance from the midsternal line to the extreme apex plus the distance from the same line to the extreme outer right border, is 13 centimeters and the transverse chest diameter is 30 centimeters, the cardiothoracic ratio would be about 43 or 43 per cent. The normal limits of the cardiothoracic ratio are between 36 and 57 per cent, with an average of about 50 per cent

This method of measurement is extremely inaccurate for it depends on only one diameter of the heart, in the frontal plane In reality, even in that plane this diameter varies markedly with the position of the heart in the chest and with changes in respiration Besides, the heart has length and depth which must be taken into consideration in determining its actual size Several other measurements are consequently often used, two of which are worthy of mention One is the long diameter, extending from a point at the junction of the right auricle and the great vessels on the right border, to the cardiac apex on the left The other is the broad diameter, consisting of the sum of two perpendiculars dropped from the long diameter—one to the right border at the junction of the right auricle and the diaphragm, and the other to the pulmonary artery on the left border. These are illustrated in Figure 37

The lengths of these three diameters, considered to be within normal range for adults are as follows·

Transverse diameter, 12 centimeters, with limits of 9 5 to 14.5 centimeters; *long diameter*, average 13 2 centimeters, with limits of 11 5 and 15 0, *broad diameter*, 9 9, with limits of 9 3 and 10 5 The last two, like the transverse diameter, are also only frontal measurements and suffer from the same faults as the latter

Newcomer and Newcomer[9] suggested the use of the rectangle figure of the heart, determined by multiplying its long by its broad diameters in relation to the rectangle of the lungs, determined by multiplying their length by their width. The normal ratio is 20 to 26 per cent with an average of 23 per cent. This is a more accurate determination but it also depends upon the frontal plane only

The transverse heart diameter, however, may, in many cases, be used with favorable results if compared with certain prediction tables that have been developed in recent years These are the outgrowth of calculations based on measurements not only of the frontal but also of the saggital diameters of the heart in relation to the height, weight and age of the individual Such determinations were first made by Rohrer[10] and later independently by Kahlstorf[11] In many cases, the results of the measurements were corroborated by making actual plastic models of the hearts and determining their volumes.

He has also seen many other cases where the heart was considered abnormal roentgenologically but nothing indicated the presence of such a condition, clinically.

REFERENCES

[1] Edeiken, J A comparison of the orthodiagram with the teleoroentgenogram Am Heart J 20 77, 1940

[2] Sabat, B Uber ein Verfahren des Roentgenographischen Dorstellung der Bewegungen des Zwerchfells, des Herzens, der Aorta Lwowski Tugodnik lekarske, 6 Nv 28, 1911

[3] Strumpf, P Das Roentgenographische Bewegungsbild und seina Amovendung (Flachenkymographie und Kymokopie) Leipzig, G Thiame, 1931.

[4] Gubner, R, Crawford, J H, Smith, W A, and Ungerlieder, H. E · Roentgenkymography of the heart Am Heart J 18 729, 1939

[5] Keys, A, Friedell, H L, Garland, L H, Madrazo, M F, and Rigler, L. G The roentgenkymographic evaluation of the size and function of the heart Am. J. Roentgenol 44 805, 1940

[6] Wolferth, C C., and Margolies, A Movements of roentgenopaque deposits in heart valve areas Am J M Sc 197 197, 1939

[7] Robb, G P, and Steinberg, I A practical method of visualization of the chambers of the heart, the pulmonary circulation and the great vessels in man J Clin Investigation 17 507, 1938

[8] Boone, B R, Chamberlain, W E, Gillick, F G, Henny, G C., and Oppenheimer, M J Interpreting the electrokymogram of heart and great vessel motion Am Heart J 34 560, 1947

[9] Newcomer, E, and Newcomer, N B Heart measurements Radiology 27 521, 1936

[10] Rohrer, F Volumbestimmung von Korperhoheen mid Organen auf Orthodiagraphischein Wege Fortschr a d Geb d Rontgentrahlem 24 285, 1916

[11] Kahlstorf, A Weber eine Orthodiagraphische Herzvolum enbestimmung Fortschr a d Geb d Roentgenstrahlen 45 123, 1932

[12] Hodges, F J, and Eyster, J A E Estimation of transverse cardiac diameter in man Arch Int Med 37 707, 1926

[13] Ungerleider, H. E, and Gubner, R Evaluation of heart size measurements. Am Heart J 24 494, 1942

CHAPTER VI

Cardiac Enlargement and Dilatation of the Great Vessels

ENLARGEMENT of the heart and dilatation of the great vessels are frequent manifestations of cardiovascular disease The nature and extent of such enlargement and dilatation are often of great aid in the diagnosis of the underlying disease, such as valvular and congenital defects, intrapulmonic and systemic hypertension, myocardial failure and so on.

CARDIAC ENLARGEMENT

Enlargement of the heart may be in the form of hypertrophy or dilatation or of both Hypertrophy alone, unless marked, is often not detected either on physical examination or roentgenologically. It may be determined only at autopsy, when the walls are found to be thicker and the weight of the heart greater than normal, as described in Chapter III. Dilatation will always present physical and roentgenologic evidence of enlargement. However, pure dilatation without some degree of pre-existing or coexisting hypertrophy is uncommon. This can be understood from the nature of the underlying causes. Hearts that show thinning of their walls at autopsy almost always weigh more than the normal for the given individual, indicating that there is an increase in muscle mass

The thickness of the wall of the heart as observed at autopsy, however, varies to a great extent with the time in the cardiac cycle when the heart stopped beating at death If during systole, the muscle wall will appear thicker, and if in diastole, thinner.

Causes The most common causes of cardiac enlargement are valvular disease, congenital defects, hypertension and pathologic states of the heart muscle resulting from coronary disease, inflammations, anemias, avitaminosis and others. The various tachycardias, if prolonged, may also produce cardiac enlargement All these will be discussed in subsequent chapters

Some enlargement of the heart may result from prolonged, extreme muscular activity If the muscular activity is continued at repeated intervals, with periods of rest between, *it will eventually lead to some hypertrophy* If, however, the activity is beyond the limit of ability of the heart muscle to carry on, some dilatation may occur

Normally, acute dilatation is prevented to a great extent by the pericardial sac which has some restraining effect. Kuno[1] observed that if the

pericardium is removed, any great increase in strain of the heart may result in heart dilatation, valvular incompetency or myocardial hemorrhage.

The effect of repeated and prolonged muscular activity upon the size of the heart is observed in trained athletes In many of them, the proportion of the heart size to body size is found to be relatively greater than in nonathletic individuals This was shown by Herxheimer[2] who made roentgenologic studies on participants in Olympic games. If the heart muscle is perfectly normal, the amount of hypertrophy resulting from muscular activity is not marked

In rare cases, no demonstrable cause of cardiac enlargement is present. Levy and Von Glahn[3] described 10 such cases and Norris and Pote[4] reported 4 cases of their own and found 13 similar cases in the literature

In a recent examination of 273 normal native Peruvians living at a high altitude, Kerwin[5] found that their hearts were generally larger than in those living at sea level. He considered it to be an adaptive change due to prolonged exposure to a low concentration of oxygen

In many cases, cardiac hypertrophy and dilatation are caused by more than one factor This is true of the more generalized forms of enlargement

Pathology The pathology of an enlarged heart varies with the kind of enlargement and with the underlying causes In some cases, the enlarged heart may have no other pathologic changes than stretching of the heart muscle and increased volume of the heart chambers in dilatation and thickening of the wall in hypertrophy In many cases, however, a variable degree of inflammatory or degenerative changes is found in addition, due to the causes mentioned above

In determining if cardiac enlargement is present, we must always bear in mind the fact that the size and weight of the heart vary normally with the size and weight of the body, as described in Chapters III and V. This relationship, however, exists only in individuals with good somatic muscular development. In fatty individuals, with poor muscular development, the heart is usually smaller in relation to body weight.

The heart may, in certain diseased states, increase to tremendous proportions. Usually the largest hearts are those that show both hypertrophy and dilatation, with the latter predominating In some cases, the greatest enlargement occurs in one chamber such as the left auricle in mitral stenosis with auricular fibrillation Here the chamber may extend across the posterior mediastinum to the right as well as to the left. In extreme degrees, the left auricle extends to the right far beyond the right auricular border and may reach the right axilla. Minkowski[6] reported the largest heart on record. The left auricle had a capacity of 3 liters. If we realize that normally, the total volume of blood that all the chambers of the heart combined can hold is about 560 cc., according to Hochrein,[7] and that the

left auricle holds only about 149 cc, we can appreciate the extent of the enlargement. Several other extremely large hearts have since been reported The latest of these was recently reported by Parsonet and co-workers[8] where the heart weighed 1600 grams

The greatest generalized enlargement occurs in multivalvular disease and in chronic adhesive pericarditis

Hypertrophy of the wall of any chamber is due to an increase in the thickness of the individual muscle fibers, not to an increase in the number of fibers. This was demonstrated by Karsner and co-workers[9] who made measurements of the size of muscle fiber in a normal heart, weighing 300 grams, an hypertrophied heart, weighing 500 grams and in an atrophied heart, weighing 165 grams. The ratio was 5.9:4, respectively

Of great importance in the process of the development of cardiac muscle hypertrophy is the fact that the capillary blood supply to the muscle fibers becomes relatively smaller as hypertrophy progresses This was clearly demonstrated in rabbits by Shipley and co-workers[10] and in the human by Roberts and Wearn[11] The latter authors had shown that in normal children, the mean fiber diameter is 8 96 μ and the mean capillary concentration is 3,744 per square millimeter muscle tissue. In normal adults, the mean fiber diameter is 13 9 μ and the capillary concentration 3,342 In hypertrophied adult hearts, the mean fiber diameter is 19 9 μ and the mean capillary concentration 2,483. Thus, in normal childhood there is a much greater capillary supply per unit of muscle tissue than in normal adults. *In cardiac hypertrophy, the capillary supply is much lower* than in normal adults. This is due to an increase in the diameter of the muscle fibers, which pushes the capillaries farther apart, and also to diminished concentration of capillaries in proportion to the increase in the fiber diameter and heart weight The average number of capillaries per given number of fibers, however, remains about the same as in the normal, which indicates that the capillaries do not multiply during hypertrophy, to keep pace with increase in muscle mass, as in normal growth We can thus see how the diminution in the arterial supply to the muscle in hypertrophy may eventually lead to failure

The progress of development of dilatation and hypertrophy of the ventricles has been studied by Kirch[12] He considered each ventricle to consist of an *inflow* and *outflow tract.* The *inflow tracts* of the left and right ventricles extend from the mitral and tricuspid orifices, respectively, to the apex The *outflow tracts* of the left and right ventricles extend from the apex to the aortic and pulmonic orifices respectively Dilatation of either ventricle always begins first in the outflow tract It starts at the terminal portion below the aortic or pulmonic valve and progresses against the direction of the blood stream down to the apex This produces oblonga-

tion and broadening of the given ventricle, inasmuch as this tract is located between the anterior wall and interventricular septum of the respective ventricles. Later, the inflow tract becomes involved, dilatation progressing from the apex against the blood stream to the auriculo-ventricular valve of the given ventricle The enlargement thus progresses posteriorwards, the tract being located between the posterior wall and the interventricular septum of the respective ventricle

In cases where dilatation is caused by impaired contractility of both ventricles, due to myocardial disease or to coronary insufficiency or other diseased states, all parts dilate uniformly This type of dilatation, Kirch termed *myogenous* in contradistinction to the type caused by strain due to valvular disease or hypertension, which he terms *tonogenous* dilatation. In the former, broadening of the whole heart occurs with dilatation In the latter, the outflow tract of each ventricle is involved first, forming oblongation with some broadening of the given ventricle

Clinical Manifestations Both dilatation and hypertrophy are compensatory mechanisms and if slowly developed, are ordinarily asymptomatic. If dilatation develops suddenly, symptoms of congestive failure will appear, as discussed in Chapter XIII

Whether or not failure develops, cardiac enlargement, if of sufficient degree, can be recognized by physical signs, roentgenologic and electrocardiographic findings

Physical Signs: Inspection and palpation may reveal various abnormal systolic as well as diastolic bulgings, depressions and retractions of the chest wall

In hypertrophy of the left ventricle, there is a well defined apical impulse, the extent of which varies with the degree of hypertrophy and with the thickness of the chest wall. The impulse extends outside the midclavicular line, and has a heaving, resistant feel It may be seen and felt even when the patient is in the recumbent posture which does not occur in most normal individuals If the left ventricle is markedly hypertrophied, a forward thrust of the entire left precordial region may be observed We must be sure, however, not to mistake an excessive precordial heave due to augmentation of the normal heart beat caused by thyrotoxicosis, neurosis, excitement, youth and certain drugs for cardiac enlargement.

In *dilatation*, the apical thrust may become feeble or may not be felt at all, and the first heart sound is faint. This may occur also in the presence of pleural and pericardial effusion, marked emphysema, left pneumothorax, a fatty chest with large breasts and in edema of the chest wall. An apical systolic murmur which may be faint at times, and some degree of failure are frequently additional signs of dilatation.

In *right ventricular enlargement*, we often observe a diffuse systolic bulge and heave over the precordium, mainly to the left of the sternal border, due to increase in the antero-posterior diameter of the enlarged right ventricle during systole

A *ventricular aneurysm*, which usually arises in the left ventricle at the apical region, may often present a sharp localized thrust extending some distance beyond the left midclavicular line in the lower precordium At times, it may also be felt as far as the left sternal border.

In rare cases of *left auricular enlargement*, where the left auricle reaches the right chest wall, a systolic pulsation in the right midclavicular line, in the region of the fifth and sixth interspace may be observed

Abnormal precordial pulsations and bulgings may occur also in the absence of enlargement of any of the cardiac chambers This must be borne in mind in differential diagnosis. Thus, *in massive pleuro-pericardial adhesions* with retraction of the lungs, a systolic tug may be observed in the precordium during ventricular systole and bulging during diastole The latter is due to filling of the ventricles which may be partly uncovered by the retracted lung In these cases we may also notice occasionally some retraction of the lower ribs and intercostal spaces of the left axillary and interscapular regions during ventricular systole, known as Broadbent's sign. It must be remembered, however, that this sign is often due to massive cardiac enlargement rather than to pericardial adhesions

Percussion may help but does not take the place of inspection and palpation in determining the presence of cardiac enlargement. Enlargement of the heart to the right, however, may be determined only by percussion, except in the rare case of massive left auricular enlargement where also a pulsation may be observed on the right side, as stated before. Any extension of percussion dullness beyond 4.5 centimeters from the midsternal line in the fourth right interspace in broad-chested, and 3 5 centimeters in the same space in narrow-chested individuals, speaks for cardiac enlargement to the right

In left ventricular enlargement percussion dullness may extend one centimeter to the left of the maximum visible and palpable impulse

Roentgenologic Findings: Of all methods of examination, a roentgenologic study gives us the most accurate picture of generalized cardiac enlargement as well as of enlargement of the individual chambers.

Left ventricular enlargement in the earlier phases, Figure 38, when only the outflow tract is affected, is best recognized in the antero-posterior view It is manifested by a downward extension of the apex, below the outline of the left dome of the diaphragm, or by an increase in the convexity of the left ventricular border, with greater rounding of the apical region of the heart. The apex does not separate from the diaphragm, and the con-

vexity does not diminish during deep inspiration. These findings differentiate left ventricular enlargement from a transversely placed heart caused by a high position of the diaphragm. In the latter condition, the apex separates from the diaphragm and any convexity present disappears on inspiration.



FIG 38—LEFT VENTRICULAR ENLARGEMENT From a male 28 years old with rheumatic aortic and slight mitral insufficiency The transverse heart diameter, 15 5 centimeters; internal transverse chest diameter, 27 centimeters Apex extends below diaphragmatic surface.

When the inflow tract of the left ventricle also becomes enlarged, the enlargement may be best demonstrated in the left oblique view, Figure 39, by a backward and downward bulge of the lower posterior cardiac border, extending to and even partly overlapping the spinal shadow

A localized aneurysm of the left ventricle, may be determined by its abnormal bulge, which distorts the shape of that chamber, as shown in Figure 139.

Right ventricular enlargement may be recognized in the antero-posterior and right oblique views. In the former, the normal concavity between the aortic knob and the left ventricle on the left margin of the cardiac sil-

houette disappears, resulting in straightening of the left border of the heart In more advanced enlargement, the area between the aortic knob and left ventricle becomes convex, resulting in a bulge It is illustrated in Figure 40. It must be remembered, however, that a normal but hypoplastic or longitudinal-shaped heart often presents a prominence in that region which must be differentiated from enlargement In the right oblique position,



Fig 39 —Marked Left Ventricular Enlargement, Seen in the Left Oblique Position The left ventricular border extends beyond the spinal column From a male, 55 years old with arteriosclerotic, hypertensive heart disease

the normal clear triangular area between the heart and the anterior chest is diminished due to the bulging wall of the right ventricle

Marked enlargement, affecting also the inflow tract may best be recognized in the left anterior oblique position by a bulge in the lower portion of the anterior border and by lengthening of the diaphragmatic portion of the heart.

Left auricular enlargement, affecting the transverse diameter, is best determined in the right anterior oblique position with a barium filled esoph-

agus, Figure 41, which is compressed posteriorwards by the enlarged auricle. If the enlargement is in a vertical direction it may best be determined in the left anterior oblique position Early, there will be noticed a widening of the angle of bifurcation of the two bronchi, and later an upward displacement or compression of the left bronchus

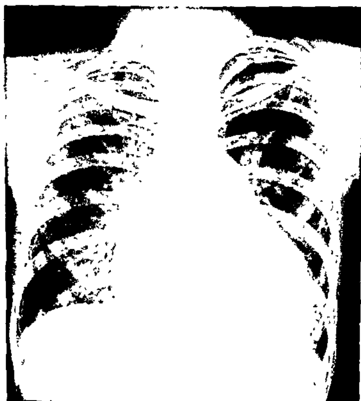


FIG 40—MARKED CARDIAC ENLARGEMENT, PREDOMINENTLY RIGHT VENTRICULAR AND SOME LEFT VENTRICULAR. From a male 26 years old with mitral stenosis and insufficiency and some aortic insufficiency The transverse heart diameter is 20 centimeters and the internal transverse chest diameter is 29 5 centimeters

In massive enlargement of the left auricle, extending beyond the right border of the heart, this border may appear as two distinct curves in the antero-posterior position, Figure 121. The upper curve is that of the left auricle and the lower, the right auricle The left auricular portion is often less dense than the right auricular

Right auricular enlargement, if slight, may be visualized in the left anterior oblique position by a bulging of the right border below the aorta. If marked, it can be visualized in the right anterior oblique position showing

encroachment of the auricular shadow upon the retrocardiac clear space above the diaphragm. A barium-filled esophagus is not compressed by this bulge inasmuch as the right auricle is to the right of and not in direct contact with the esophagus The esophagus is seen passing through the opacity of this bulge



FIG 41 —RIGHT ANTERIOR OBLIQUE POSITION Left auricular enlargement The barium-filled esophagus is compressed and pushed backwards in its lower portion by the enlarged left auricle

In marked right ventricular enlargement the auricle is displaced more or less to the right, upwards and posteriorwards and thus may simulate enlargement of the right auricle

Multiple chamber enlargement may be visualized roentgenologically in the various views showing the individual chamber enlargement.

We must always bear in mind the fact that low grade valvular disease or mild hypertension may not produce demonstrable enlargement of the affected chamber, and multiple valvular disease may produce chamber enlargement corresponding to the severity of the given valvular damage. Also, the normal configuration of the heart is so variable, that enlargement of a given chamber in some individuals may not be evident. For these

reasons, we must always correlate the roentgenologic with the clinical findings in any case to arrive at a proper diagnosis.

Cardiac dilatation of the so-called myogenous type of Kirch, not due to valvular disease is usually symmetrical. The organ appears to rest on the diaphragm in a spread-out fashion, Figure 42



FIG 42—MASSIVE CARDIAC ENLARGEMENT, PREDOMINENTLY DILATATION, LATE PHASE OF ADVANCED ARTERIOSCLEROTIC HEART DISEASE WITH LOW GRADE HYPERTENSION AND MARKED CONGESTIVE FAILURE Male, 52 years old The transverse heart diameter is 20 centimeters and the internal transverse chest diameter 30 centimeters

Electrocardiographic evidence of cardiac enlargement consists of a large, broadened and at times, a notched P wave in case of auricular enlargement, and preponderance of the right and left ventricle, if present, in relative enlargement of the respective ventricles. These have been fully discussed elsewhere.[13]

DILATATION OF THE GREAT VESSELS

Dilatation of the aorta and pulmonary artery, superior and inferior venae cavae and the main pulmonary veins may be caused by any factor that

increases the pressure in the given vessel. In the presence of degenerative or chronic inflammatory changes which weaken the vessel wall, dilatation may occur even if the intravascular pressure is not excessive.

Aortic Dilatation: Dilatation of the aorta may be diffuse or sacculated. Diffuse dilatation is usually due to increased intra-aortic pressure caused by arterial hypertension or by aortic valvular insufficiency. It may also occur in degenerative changes of the aorta without marked increase in intra-arterial blood pressure. Sacculated dilatation is due to localized pathologic changes in the vessel wall, usually syphilitic

Diffuse dilatation is always associated with elongation of the entire thoracic aorta. In fact, elongation may occur before dilatation The elongated aorta undergoes a variable degree of tortuosity in order to accommodate itself between the two points of its fixation, at the base of the heart and at the diaphragm. As a result of tortuosity, the ascending portion extends a greater distance to the right of its natural position, the transverse portion rises higher than normally, and may extend as high as the suprasternal notch, and the junction of the transverse and descending portions extends a greater distance to the left, forming the so-called knob [illegible] considerable bending, depend- [illegible]

Physical examination may reveal a visible and palpable suprasternal pulsation, and the percussion dullness in the second right interspace may extend a variable distance to the right, beyond the sternal border, depending upon the degree of tortuosity and dilatation in this direction If the dilatation is extensive, a systolic pulsation may be felt and seen in the second right interspace or over a wider area in that region.

The width and tortuosity of the entire transverse arch cannot be determined, of course, by percussion, as it runs backwards in its transverse course, and is not close enough to the anterior chest wall in its entire length.

Roentgenologic examination is the best method of determining the shape and size of the thoracic aorta in its entire length This is true especially where the vessel is sclerosed, which increases its opacity.

Dilatation and tortuosity of the ascending portion above the area covered by the right auricle assumes a variable degree of right lateral convexity in the antero-posterior view, shown in Figures 43, 44 and 45. As seen in the left anterior-oblique view, it assumes an anterior convexity.

The transverse portion is best visualized in the left anterior-oblique or left lateral views, shown in Figure 46. It is usually elevated to a considerable height and there is a marked separation of the ascending from the descending portions. The descending limb is displaced backwards from its prevertebral position to the left border of the spine or even beyond. If examined with a barium-filled esophagus, the aorta will be seen to produce

a greater indentation in the esophagus than normally. Frequently the esophagus is seen to be pulled to the left below the aortic indentation due to the fibrous attachment between the esophagus and aorta at this level, in many cases The trachea may be pushed over to the right and the bronchi may show a wider separation at their bifurcation.

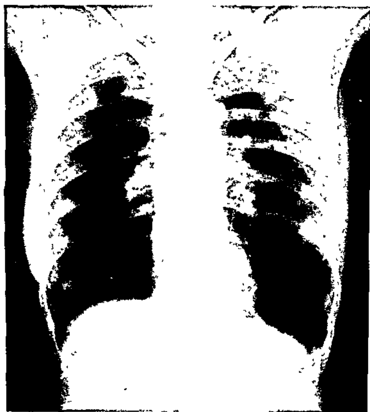


FIG 43—MODERATE DILATATION AND TORTUOSITY OF THE THORACIC AORTA The heart and aorta are of longitudinal shape No evident enlargement of the heart. From a female, 57 years old, with long-standing hypertension

The *descending portion* may be observed in the antero-posterior and in the left or right anterior oblique positions. It may assume sinuous curves, the left Calcification may oc- vell as at the knob.

Sacculated dilatation or aneurysm of the thoracic aorta may affect any part of the vessel. It is fully described in Chapter XXI.

Pulmonary Artery Dilatation: Dilatation of the pulmonary artery is due to any condition which increases the intrapulmonic arterial blood pressure.

The causes are therefore the same as those producing right ventricular hypertrophy and dilatation. In all cases, the main trunk and its branches share in the dilatation.

Dilatation of the main trunk may be determined by physical examina-



FIG 44—GREATER DILATATION AND TORTUOSITY OF THE AORTA THAN IN FIG 43 The ascending portion shows an increased right lateral curvature The transverse portion shows a greater than normal indentation of the barium-filled esophagus The knob shows a streak of calcification The descending portion shows a left lateral curvature From a male, 65 years, with long-standing hypertension

tion, but more accurately roentgenologically. Dilatation of the primary and secondary branches can be determined only roentgenologically.

Dilatation of the main trunk is evidenced by an increase in the area of percussion dullness in the third left intercostal space beyond the average normal of four centimeters from the midsternal line. The wider the area of dullness, the greater the dilatation Roentgenologically, some degree of bulging is seen on the left border of the cardiac silhouette in the space between the aorta and the left ventricle, in the antero-posterior view.

Dilatation of the right branch of the pulmonary artery cannot be visual-

ized roentgenologically but dilatation of its secondary branches is shown in the antero-posterior view by an increase in the size of the right hilar shadow. Expansile pulsation of these vessels may be observed in occasional cases Dilatation of the left branch of the pulmonary artery may occasionally be seen in the left oblique position by a widened streak of increased density crossing the left bronchus



FIG 45—MORE DIFFUSE DILATATION OF THE THORACIC AORTA THAN IN FIG 44 The barium esophagram shows a somewhat wider indentation There is also moderate cardiac enlargement From a female, 60 years old, with long-standing hypertension

Dilatation of the Venae Cavae: This may occur in right heart failure or in local obstruction to the flow of blood from these main venous trunks into the right auricle The latter may be caused by local pericardial adhesions, tumors and so on. Dilatation of the inferior vena cava cannot be determined The condition may be suspected when we observe marked *venous dilatation and increased* venous pressure in the lower part of the body. Dilatation of the superior vena cava may be determined roent-

genologically in the antero-posterior view. It appears as a vertical shadow extending laterally and above the ascending aorta It is also associated with dilatation and increased pressure of the veins in the neck, head and chest.



FIG. 46—LEFT LATERAL VIEW WITH SLIGHT INCLINATION ANTERIORWARD; SAME PATIENT AS IN FIG 45. The transverse aorta is elevated with marked separation of the ascending from the descending portions

Dilatation of the Pulmonary Veins This cannot be detected by physical or roentgenologic examination. It is assumed to be present in any condition where an increase in the pulmonary venous pressure is expected to occur, as in mitral stenosis and left heart failure.

DIFFERENTIAL DIAGNOSIS

Dilatation of the heart and great vessels is often difficult to differentiate from mediastinal tumors lying close to the heart, aorta and pulmonary artery Careful roentgenologic study in various positions is often essential

to arrive at a diagnosis Even then, it may at times be hard to differentiate the two conditions. This is especially true where the tumor is freely movable and lies very close to the heart or the great vessels, so that the pulsations are transmitted to it In some of these cases, angiocardiography may be the only means of differential diagnosis.



FIG 47—CHEST DEFORMITY DUE TO EXTREME KYPHOSCOLIOSIS OF THE DORSAL SPINE The heart shadow merges with the spinal shadow The barium-filled esophagus is markedly displaced to the right in its lower portion The aortic indentation is seen in its upper portion Female, 59 years old, with arteriosclerotic heart disease and complete heart block

Pericardial effusion, both the diffuse and the localized encapsulated forms, may offer difficulties in differentiating from cardiac enlargement The subject is fully dealt with in Chapter XXV.

Displacement of the heart may at times be mistaken for enlargement. There should ordinarily, however, be no difficulty in differentiating one from the other. In displacement, the heart is moved over from its usual position and some underlying causes such as spinal deformity, pneumothorax, pulmonary atelectasis or massive adhesions are usually found. *Spinal deformity, if extreme, may at times produce not only displacement* of the heart but also an opacity which merges with the cardiac shadow

and which makes it difficult to delineate the heart borders, roentgenologically, as shown in Figure 47.

REFERENCES

[1] Kuno, Y.: The significance of the pericardium. J. Physiol 1 1, 1915.

[2] Herxheimer, H : Das Herz und die Körperarbeit Klin Wchnschr 11 92, 1932.

[3] Levy, R L , and Von Glahn, W. C Cardiac hypertrophy of unknown cause A study of the clinical and pathological features in ten adults Am Heart J 28 714, 1944.

[4] Norris, R. F., and Pote, H H Hypertrophy of the heart of unknown etiology in young adults: Report of four cases with autopsies Am Heart J 32 599, 1946

[5] Kerwin, A J Observations on the heart size of natives living at high altitudes Am. Heart J. 28 69, 1944

[6] Minkowski, K Demonstration ūnes Herzens mit Ungewöhnlich Starker Dilatation der Vorhöfe. Munch Med Wchnschr 51 182, 1904

[7] Hochrein, M Untersuchungen am venösen Teil des Kreislaufes I. Herzkapozität Arch f exp Path 124 343, 1927

[8] Parsonnet, A. E , Bernstein, A , and Martland, H S Massive left auricle with special reference to its etiology and mechanism Report of a case Am Heart J 31:438, 1946

[9] Karsner, H T , Saphir, O , and Todd, T W The state of the cardiac muscle in hypertrophy and atrophy. *Am J Path 1 351, 1925*

[10] Shipley, R. A , Shipley, L J., and Wearn, J T The capillary supply in normal and in hypertrophied hearts of rabbits J Exper Med 65 29, 1937

[11] Roberts, J T , and Wearn, J T Quantitative changes in the capillary muscle relationship in human hearts during normal growth and hypertrophy Am Heart J 21 617, 1941

[12] Kirch, E . Ueber das Zustandekommen der Physiologischen und Pathologischen Sogenannten Sportherzens Ztschr f Kreislauff 20 132, 1928

[13] Sigler, L H The Electrocardiogram, Its Interpretation and Clinical Application New York, Grune & Stratton, 1944 Pp 282–301

CHAPTER VII

Heart Rate and Rhythm: Normal and Abnormal

THE RATE and rhythm of the heart are frequently normal in the presence of heart disease The occurrence of a normal rate and rhythm in a given case can, therefore, not be used as definite criteria of the absence of such disease On the other hand, abnormalities in the rate and rhythm of the heart almost always indicate either the presence of some constitutional disturbances or disease of the heart or both. In many cases, the constitutional disturbances or the heart disease may be easily diagnosed. In some cases, however, they may not be detectable.

Disturbances in heart rate and rhythm are often temporary phenomena and may be of no clinical importance. They may occur in apparently perfectly normal individuals and no ill effects follow Furthermore, in some cases, they may recur from time to time for many years and between the attacks the person may feel perfectly well

We shall attempt to present here the normal heart rate and rhythm and the clinical features of the various tachycardias and arrhythmias The electrocardiographic manifestations have been fully described elsewhere [1]

NORMAL RATE AND RHYTHM

The normal rate and rhythm of the heart consist of orderly contractions of the auricles and ventricles due to impulses elaborated in the sino-auricular node and propagated to the auriculo-ventricular node and to the lower conduction apparatus in the ventricles The elaboration and discharge of these impulses, and, therefore, the heart rate, varies in adults normally between 72 and 78 per minute, and the rhythm is practically regular. We often find, however, normal adults whose heart rates are 90 beats per minute or slightly more. There are others where it is as low as 60 or less beats per minute. In the latter there is also some degree of sinus arrhythmia.

The heart rate is slightly faster in the average female than in the male It is much faster in infancy and youth where we normally observe also marked sinus arrhythmia. The normal rates at birth and the first six months of life vary between 125 and 145. Between six months and twelve months, it is about 110 and 130. Between one and two years of age, it is about 110 and 120. Between two and four, 100 to 115. Between 4 and

6 years, 95 to 105. Between 8 years and adolescence it varies between 80 and 90.

All these are more or less basal rates, obtained while the person is in a quiescent or restful condition Any excitement or physical strain will raise the heart rate considerably. The extent of such rise will correspond to the degree of excitement or strain. Change in posture from an upright to a recumbent position for a short period of time will slow the heart rate, and slowing will be more marked after prolonged rest, and especially during sleep.

Abnormal Rate and Rhythm

Abnormal acceleration or slowing of the heart and disturbances in rhythm may result either from a pathologic acceleration, a decrease or an irregular rate of the impulse formation in the sinus node, or, from the onset of ectopic impulses arising in other parts of the heart, or, from disturbances in conduction between the auricles to the ventricles Most of these abnormal conditions can be easily recognized clinically. In many cases, however, the electrocardiogram is essential for a proper diagnosis

Sinus Tachycardia, Bradycardia and Arrhythmia

Abnormal sinus acceleration and slowing of the heart and sinus arrhythmia are sometimes spoken of as homotopic or homogenetic acceleration, slowing or arrhythmia, because the impulse originates in the normal sinus region, and is propagated along its normal course to the ventricles.

Sinus Tachycardia Sinus tachycardia may be said to exist in any case where the heart rate is above 90 beats per minute in adults and more than 10 beats above the maximum normal for the given age in childhood, and where it varies considerably with change in posture and increases after exercise. The degree of tachycardia depends upon the extent of increase in rate. The highest rate in sinus tachycardia in adults is 160, although occasional cases are encountered where the rate is higher. In some cases, it may be temporarily slowed by the carotid sinus reflex

Under normal conditions, transient sinus acceleration of the heart occurs as a result of exertion and excitement. Exertion, if not carried out beyond endurance, may accelerate the heart rate 15 to 35 beats per minute above normal and the rate will return to the original level in 2 minutes or less. The increase in rate and its slowing at rest are due to the effect of the vagus and sympathetic nerves upon the production of impulses in the sinus node. Increased demand for blood supply due to greater metabolic activity results in stimulation of the sinus node through the sympathetic system accelerating the impulse formation and discharge. Rest diminishes metabolic activity and thus sympathetic stimulation, and increases the

vagal effect which slows the impulse formation in that node. In *normal conditions*, the vagus nerve is therefore conservative and protective to the heart.

Certain drugs such as amyl nitrite, adrenalin, thyroid and caffein also temporarily accelerate the heart by stimulating the sympathetic Large doses of atropin or belladonna increase the heart rate by paralyzing the vagus

In pathologic conditions, sinus tachycardia occurs in emotional and nervous disturbances, in certain intoxications, particularly thyrotoxicosis, in infections and infarctions in any part of the body Some chronic infections may be afebrile and tachycardia may be the only or the main manifestation of the condition. This may be true also of infarction These conditions should be looked for if there is no other demonstrable cause to explain an existing tachycardia

In any unexplainable sinus tachycardia, we must always rule out neurosis as a possible cause This can be done by counting the pulse rate during sleep, as suggested by Struthers and Bacal [2] A drop of 10 to 20 beats per minute during sleep would help rule out organic disease as a cause.

In acute infectious disease, the average rise in the heart rate above normal is approximately 8 beats per minute for each degree of fever In some cases, however, the acceleration in the heart rate far exceeds the elevation in temperature This is true especially in tuberculosis and in rheumatic fever On the other hand, in certain infectious diseases such as typhoid and meningitis the heart rate may be relatively slow

In some postfebrile conditions, tachycardia may persist a long time after all other signs of infection have subsided This is true especially after influenza. In such cases, we must always suspect that heart damage may have been produced by the infectious state, and the patient must be kept under careful observation

Sinus tachycardia is encountered in traumatic injuries or hemorrhage, except in cases where the base of the brain is involved when sinus bradycardia may occur

Sinus Bradycardia Sinus bradycardia is said to exist in any case where the rate is definitely slower than the minimum normal for the given age and varies with change in posture and physical activity The condition is caused by increase in vagal tone, and may be a temporary phenomenon or a permanent state

As a temporary phenomenon, it may occur as a result of sudden increase in blood pressure which stimulates the carotid sinus and aortic regions, producing reflex vagal slowing of the heart and a tendency to lower the pressure. In individuals with a hyperactive carotid sinus reflex, pressure upon the carotid sinus region will produce marked slowing and even stoppage of the heart for as long as 2 or 3 minutes, and may result in syncope

and convulsions, as previously described[3, 4] This reflex occurs more frequently and is more marked in individuals showing evidence of coronary insufficiency and the author has therefore advocated this test as one of the diagnostic criteria of coronary disease.[5]

Sinus bradycardia occasionally occurs in cholelithiasis, during colic induced by the passage of a stone It is also caused by other reflex vagal irritation arising in the abdominal viscera

More prolonged sinus bradycardia, lasting as long as the underlying disease which produces it, occurs in disease of the basal portion of the brain such as infections, arterial thrombosis or hemorrhage as well as in brain tumors. All these produce irritation of the vagal nuclei It also occurs in marked jaundice due to any cause It is a prominent feature also in hypothyroidism and in Addison's disease Any other constitutional state which depresses the metabolic activity of the body such as starvation and profound sleep will produce sinus bradycardia

As a more or less permanent manifestation, sinus bradycardia may occur in some perfectly normal individuals, of the so-called vagotonic type The author has observed several normal young males whose heart rates normally ranged between 30 and 50 beats per minute It is also seen in some athletes Some of these, however, may show, from time to time, periods of sinus tachycardia, indicating general instability of the vago-sympathetic system

Sinus bradycardia is a frequent finding in elderly people. In some of these, the cause may be a diminution in the blood supply to the sinus node due to coronary disease In most cases, it is probably due to vagal effect resulting from the lower metabolic condition incident to age It may therefore be considered a protective mechanism

Sinus Arrhythmia. Irregularity in the formation of the sinus impulse in the heart is caused by transient increase and decrease of vagal inhibition Inasmuch as it is most often induced by a reflex respiratory effect on the vagus, it is also known as respiratory phasic or vagal arrhythmia Occasionally, this irregularity may result from other reflex effects on the vagus such as deglutition. In exceptional cases, sinus arrhythmia occurs spontaneously without any known reflex stimulation In such cases, if the arrhythmia is marked and frequently recurring, and especially if a considerable degree of sinus bradycardia is also present, it may be due to grave organic disease of the brain or of the vagus nerve itself, such as vagus neuritis.

In childhood and early adult life, sinus arrhythmia is a frequent manifestation. In fact, according to Mackenzie,[6] it is a sign of a healthy heart, and when it occurs after an infectious disease that affected the heart, it is a sign of recovery.

In individuals of the arteriosclerotic age, sinus arrhythmia is an abnormal

phenomenon, and is often associated with coronary insufficiency. This is particularly true when the sinus arrhythmia is not phasic and comes on spontaneously without known reason. The author has recently observed a female, 72 years old, who developed symptoms suggestive of acute coronary occlusion. The electrocardiogram was normal except for marked, nonphasic, sinus arrhythmia She died suddenly two days after the attack. Death was probably caused by sudden cessation of the impulse formation in the sinus node

In normal conditions, sinus arrhythmia entirely disappears on acceleration of the heart by exercise or other factors.

Treatment of Sinus Tachycardia, Bradycardia and Arrhythmia

The treatment of these conditions consists of the removal of the underlying causes when possible There is no drug that will permanently change the rate and rhythm in these cases, as long as the underlying causes are operative

Ectopic Tachycardia, Bradycardia and Arrhythmia

In this group are included disturbances in the rate and rhythm of the heart caused by impulses originating in other parts of the heart. The most important conditions belonging to this group are premature or ectopic contractions, nodal rhythm, paroxysmal tachycardia, auricular flutter and auricular fibrillation

Ectopic or Premature Beats

This is the most common form of disturbance in the cardiac mechanism It is characterized by the interruption of the normal rhythm by beats originating in other parts of the heart. This condition may also occur in conjunction with other arrhythmias such as auricular fibrillation

The site of origin of these ectopic beats may be in the auricles, junctional tissues or ventricles In rare cases it may originate in the lower portion of the sinus node itself

The focus of origin of the impulse may best be determined by the electrocardiogram, but it may also be approximately determined by auscultation. Thus, an ectopic beat, being premature, follows the normal heart beat earlier than the regular run of beats in the given individual. If the ectopic beat originates in the auricles, the interval between normal beat and the premature contraction is shorter than usual, but that between the premature contraction and the next normal impulse is approximately the same as between two normal contractions.

If the impulse originates in the junctional tissues or in the ventricles, the interval between the premature contraction and the next normal con-

traction will be much longer than that between two normal contractions This abnormally long interval is spoken of as a "compensatory pause." Thus, the length of the postectopic interval is a fair index of the origin of the ectopic beat. The reasons for these differences are given elsewhere [1]

Causes: Premature contractions often occur in perfectly normal individuals without any known cause In others, they may be traced to gastro-intestinal disturbances, to chronic focal infections, to chronic gall bladder disease, to the excessive use of tea, coffee, tobacco, alcohol and the various drugs, notably digitalis, ephedrine, calcium, barium chloride and others They may occur after nervous and mental excitation and during rest after physical work They often occur during operations, especially on abdominal viscera, due to reflex vagal irritation and as a result of anesthesia

This arrhythmia occurs more frequently in the presence of organic heart disease, especially the arteriosclerotic type Its appearance for the first time after 40 years of age should, therefore, make us suspect the presence of coronary sclerosis. This is particularly true if the premature contractions are frequently-recurring or come on when the heart is accelerated by exercise or by other causes. In normal individuals, acceleration of the heart usually abolishes premature contractions. We must bear in mind the fact that structural damage to the heart of microscopic dimensions may be sufficient to act as a focus of irritability and ectopic impulse formation. Hence, the only evidence of such a small amount of damage may be this disturbance.

Symptoms. In many cases, ectopic beats may occur without any subjective symptoms. The disturbance may be discovered accidentally on examination. In such cases, the patient may first become aware of its presence when the physician, through carelessness or improper understanding of the nature of the disturbance, informs him of the presence of heart disease or abnormality Occasionally, the patient himself may discover the irregularity, even though it may not produce any symptoms

In some patients, the premature contractions do produce abnormal sensations which bring them to the doctor for examination. Some complain of a feeling of a "thump" or a "twist," as if "the heart is turning over." Others have a feeling as if "the heart stops momentarily." Still others may complain of a momentary "thump" or "pressure" in the head, neck or in the remote parts of the body. If the premature contractions are frequently recurring, the patient may experience dizziness, fainting sensation and severe palpitation and "weak spells." Some patients complain of the recurrence of "heavy beats with stoppage and terrific thumping" In occasional sensitive individuals, there may be some precordial pain.

Disturbances in the Hemodynamics The various abnormal sensations are due to disturbances of the circulation during the premature contractions, particularly if they are of the ventricular type A sudden premature contraction of the ventricles during diastole closes the auriculo-ventricular valves before the auricles have fully emptied Temporary stasis in the auricles and a rebound systolic impulse is thus transmitted to the veins. This in some sensitive patients is responsible for the sensation of thumping in the head and neck. If the premature contraction occurs very early in diastole, it will eject very little, if any, blood into the arterial circulation Only during the normal beat following the long compensatory pause will the arterial circulation receive a large stroke volume. In fact, that stroke volume will be larger than normal because of the greater amount of blood that accumulated in the ventricles during the compensatory pause Thus, there will be temporary disturbances in the volume distribution of blood in the peripheral arterial system which in sensitive individuals will express itself in abnormal sensations in distant parts of the body Kline and Bidder[7] observed in 11 cases that the abnormal sensations were felt during the premature beat itself, not during the pause or the large beat following.

Objective Findings These consist of variations in the heart sounds, in the character of the pulse and in the blood pressure readings.

The *variations in the heart sounds* in premature contractions depend upon the origin of the premature contraction and the time of its appearance. In an auricular premature contraction, which appears before ventricular systole has ended, no first heart sound is heard as the blood in the auricles cannot enter the ventricles In such cases, an extra auricular wave will appear in the veins of the neck and an extra P wave in the electrocardiogram Any premature contraction occurring in the ventricular diastole, but before a sufficient amount of blood entered the left ventricle, will produce a first sound but no second sound This first sound is caused by vibrations set up by the contracting ventricles during the early rapid inrush of blood from the auricles Because of the small volume of blood in the ventricles, the intraventricular pressure will not be high enough to open the semilunar valves, hence no second sound will occur. Auscultation of the heart in such cases yields a normal first and second sound followed by a third sound caused by the premature contraction. This third sound may, at times, resemble a normal third sound, from which it is differentiated by the compensatory pause which follows the premature contraction, and by its appearance only at certain periods, not regularly.

If a ventricular premature contraction occurs later in diastole, when a sufficient amount of blood has entered the ventricles, it will produce a loud first and comparatively weaker second sound. The loud first is prob-

ably due to the unusual vibrations set up in the ventricles because of disparity in the contraction time of each ventricle and unequal closure of the auriculo-ventricular valves on both sides The weaker second sound is due to the smaller volume of blood entering the aorta during the premature contraction, resulting in lower intra-arterial pressure and thus in a less forceful closure of the semilunar valves

The character of the pulse resulting from a premature beat also depends upon the period in diastole when the premature beat occurred. If it occurs very early, there will be no pulse A long gap will be felt between two normal pulses, which may be mistaken for a dropped ventricular beat due to heart block or transient stoppage of the whole heart due to sino-auricular standstill. This can be differentiated by listening to the heart during the absence of the pulse when the extra heart sound of the premature contraction will be heard If the premature contraction occurs later in diastole, its pulse felt in the radial artery will be weaker and appear later than normal and its blood pressure reading will be lower, due to the fact that the volume of blood it sends out into the arterial tree is smaller

Premature beats often recur, and at times assume special characteristics Thus, they may recur after every normal beat when they are spoken of as *pulsus bigeminus* or they may recur after every third normal beat, spoken of as *pulsus trigeminus* and so on. If they recur after every normal beat, the type of pulse they produce may be mistaken for pulsus alternans The differentiation may be easily made by listening to the heart, when heart sounds due to premature contractions may be heard

Occasionally, a premature contraction may occur between two normal beats, not disturbing the basic rhythm. The condition is spoken of as *interpolated premature contractions* In such cases, three groups of first and second heart sounds will be heard, the middle group being somewhat weaker The group of sounds is not followed by a compensatory pause. The pulse will also show such grouping, the first pulse being stronger

Occasionally, premature contractions may recur one after the other in groups of two or more Such a condition is usually a precursor of more serious disturbances such as ectopic tachycardia, fibrillation and flutter.

Treatment In cases where premature contractions are asymptomatic and are discovered accidentally by the physician, no therapy is necessary. It is absolutely essential, however, that the patient is not informed of the existence of the arrhythmia In all cases, and particularly in those where the arrhythmia is associated with subjective disturbances, the underlying cause must be looked for and removed if possible This is the only definite way to overcome this irregularity. Drug therapy is usually of little value in this condition. Some patients, however, may respond to quinidine sulphate in doses of 3 to 6 grains every four hours. This should be tried

only if the cause if not discoverable or removable. In the neurogenic cases the sedatives, especially bromides and phenobarbital, may be of help if the arrhythmia is disturbing. The bromides may be given in 15 grain doses and phenobarbital in ¼ to ½ grain doses three times a day. In cases where the arrhythmia occurs in severe myocardial disease with failure, it may disappear on the improvement of the heart under digitalis therapy

Nodal Rhythm

This is a comparatively infrequent condition occurring at times after a febrile state, in local circulatory disturbances or inflammatory changes of the auricles, especially in the region of the sino-auricular node, and in some intoxications, especially digitalis Because of the depression of the activity in the sino-auricular node, the auriculo-ventricular node or the bundle assumes leadership of the heart. In rare cases, both the sino-auricular as well as the auriculo-ventricular nodes are active, the auriculo-ventricular node being more so, produces impulses at a somewhat faster rate The condition is best recognized by the electrocardiogram and has been fully described elsewhere.[1]

This abnormality is characterized clinically by a slow heart rate, although in occasional cases, the rate may be normal or even slightly higher than normal There may be no subjective disturbances, although in sensitive individuals, there is occasionally a feeling of palpitation or throbbing in the neck This is probably due to the pulsation transmitted to the veins caused by simultaneous contraction of the auricles and ventricles Treatment consists of removing the cause

Paroxysmal Tachycardia

This form of tachycardia consists of rapidly recurring premature contractions As such, it originates from an *ectopic* area of the auricles, junctional tissues or ventricles We thus recognize auricular, junctional and ventricular forms of paroxysmal tachycardia In rare cases, it appears to arise in the sinus node itself Inasmuch as in the vast majority of cases the disturbance arises in regions other than the sinus node, the term *ectopic tachycardia* is often employed

The Physiologic Mechanism. The disturbance is considered, today, to be caused by the same mechanism as auricular flutter and fibrillation, namely, a circus movement In paroxysmal tachycardia, part of the path goes through a node which slows the rate of travel of the circus This was shown by Barker and co-workers.[8] The unity of these conditions was recently stressed by Evans [9]

Characteristics. Paroxysmal tachycardia begins and ends abruptly and the rate is not influenced by change in posture or by exercise The usual

rate is 160 to 180 beats per minute, although rare cases are found where the rate is as low as 110 or even lower and as high as 200 or more. Each attack may last a few seconds or minutes or many hours, days, weeks or months The author has under observation, a female child, 9 years old, who has been having a continuous auricular tachycardia with a rate of 160 beats per minute for the past three years, without intermission, and is not influenced by any of our available means of therapy except for some slowing of the rate by large amounts of digitalis.

The Causes The disturbance appears to be due to the same factors as those causing premature contractions, and as such, is not ascertainable in many cases. The auricular form which is the most common, comprising *perhaps about 75 per cent of cases of paroxysmal tachycardia, most often* occurs in individuals who have no demonstrable evidence of organic heart disease. This may be true also of the rarer junctional form On the other hand, the ventricular form is, in most cases, associated with organic heart disease Even the auricular or junctional forms, however, have a tendency to occur more frequently in the presence of mitral stenosis and thyrotoxicosis where auricular fibrillation and flutter are frequent occurrences.

Subjective Sensations· These consist of sudden and abrupt onset of palpitation and a peculiar fluttering feeling in the precordium In some cases, the disturbances may be felt only at the onset and termination of the attack while during the attack itself, the patient may be comparatively free from symptoms Some patients complain of fluttering feeling in the head, abdomen and extremities Many complain of dizziness, headache, *faintness and marked weariness With an extremely rapid heart rate,* which greatly shortens the diastolic period and diminishes the stroke and minute volume output of the heart, syncope and in rare cases even convulsions may occur In prolonged tachycardia with a very rapid rate, signs of cardiac failure will ensue, if not checked

In some cases, especially in sensitive individuals or in those who have coronary sclerosis, an attack may be associated with precordial pain or the anginal syndrome The author has recently observed a man 53 years of age who was subject to recurring attacks of auricular paroxysmal tachycardia for twenty-eight years Up to about 50 years of age he had no serious subjective disturbances other than a "feeling of heat over the body at the onset, cold at the termination and some fluttering during the attack" Since 50 years of age, however, during each attack he was subject to the anginal syndrome, which was getting progressively more severe as the attack persisted At times the symptoms simulated those of coronary occlusion

Objective Findings· The patient may look more or less apprehensive and may have some pallor during the attack. If the heart rate is not extremely fast the heart sounds may be fairly normal, the pulse of good quality and the blood pressure normal If the heart rate is above 160 and especially if in the neighborhood of 200 or over, the first heart sound becomes shortened and the two sounds assume a tick-tack quality The pulse becomes very weak and at times imperceptible and the blood pressure falls to a very low level. Occasionally pulsus alternans may develop If the condition persists, signs of congestive failure ensue

The main characteristic of the heart rate is that it does not change materially from time to time and on change in posture. This is true particularly in auricular tachycardia. In ventricular tachycardia, there may be a difference at times of several beats from minute to minute This point may be used in differentiating ventricular from auricular tachycardia

Treatment In many cases of supraventricular tachycardia the attacks may be terminated abruptly by any mechanical means that produces reflex stimulation of the vagus. The best method is rapid and firm compression of the carotid sinus area by the thumb In some cases the response is dramatic, occurring almost instantaneously In others, the compression has to be continued with slight massaging movement of the thumb for about one half to one minute The compression should be localized to the exact area of the carotid sinus located at the bifurcation of the carotid artery at the level of the cricoid cartillage, as described in Chapter XV It should be tried first on the right side and if unsuccessful, on the left side.

A word of warning must be given in the use of this method. In individuals of the arteriosclerotic age, with evidence of cerebral or coronary sclerosis, serious consequences may occasionally follow this method, such as an acute cerebral vascular accident or complete cardiac asystole Although these conditions rarely occur, they should be borne in mind when treating an individual in the older age group.

In an occasional case, a paroxysm may be arrested by compression of the eyeball. Often the patient himself learns to stop the attacks by assuming certain positions, such as lying on the back with arms stretched out, bending down, forced expiration with the glottis closed, holding the breath, rapid and deep inspirations and various other means. The induction of vomiting by putting the finger in the mouth and touching the uvula or the posterior pharynx, or by large doses of ipecac, occasionally terminates an attack.

If any of these methods fail we must resort to certain drugs. The best and most reliable of these is quinidine sulphate. This drug may be used also as a prophylactic measure to prevent the recurrence of an attack after

it has been terminated by any means. It is also of great value in ventricular paroxysmal tachycardia.

The dosage of quinidine used to stop an attack varies in different individuals. Inasmuch as some cases show marked sensitivity to the drug, it is advisable to start with an initial dose of 3 grains, given by mouth, and to watch for about two hours for any toxic effects. These may consist of dizziness, palpitation, vomiting, epigastric distress, tinnitus or headache. When these symptoms appear, the drug should be discontinued. Further use of the drug in large amounts in such cases may be followed, in some instances, by marked accentuation of these symptoms and in an occasional case by syncope, convulsions, respiratory failure and death. Less serious, but annoying disturbances may consist of urticaria, eczema, diarrhea and febrile reactions.

When it has been ascertained that no untoward effects occur after the initial dose, which is true in the vast majority of cases, six grains is to be given every two to four hours until the attack subsides, or until some of the toxic symptoms become evident. The frequency of repetition of the dose depends upon the severity of the attack and reactions of the patient. In an occasional case as little as the initial dose of 3 grains is enough to bring about a cessation of the attack. In such cases a similar maintenance dose may be given every four hours for several days to prevent a recurrence of the attack. In other cases, showing resistance to the drug, as much as 40 to 50 grains per day may be necessary to break the attack. However, such doses are very seldom required, and it is perhaps unwise to exceed them. Cases that do not respond to the larger doses will probably not respond at all. When the paroxysm ends, it is necessary to continue the use of the drug in 3 grain doses every four hours for three days and nights, and later, three times a day for a week or two, depending upon the frequency and severity of occurrence of the attack in the given case.

In cases of great urgency, especially in ventricular paroxysmal tachycardia, or in all cases which are resistant to treatment, the drug may be administered intravenously. The safest preparation for that purpose is quinine dihydrochloride which is available in ampules of $3\frac{3}{4}$ grains each and which should be diluted in 20 cc. of sterile, distilled water and injected extremely slowly, until a return to normal rhythm occurs or until a maximum of $7\frac{1}{2}$ grains is injected. The intravenous method of administration is far more dangerous than the oral method.

The concentration of the drug in the heart and its elimination from the body vary with the dosage. Weisman[10] found that a single 100 mg. dose given to a dog by mouth resulted in a maximum concentration of the drug in the heart in thirty minutes and no trace was found at the end of four hours. When a single dose of 585 mg. was given, the maximum concentration was reached in about one hour and it took seven hours for the

last trace to disappear from the heart. When repeated small doses were given at one hour intervals the maximum concentration of the drug in the heart was reached in about one hour when only two doses were given, and in about three hours when three or four doses were given, one hour apart. Very little remained in the heart at the end of five hours.

Delevett and Poindexter[11] studied the plasma concentration of quinidine in two patients who received the drug for the treatment of nodal paroxysmal tachycardia They observed that if the concentration was less than 1 mg per liter of blood, paroxysms recurred. There was a marked individual variation in the plasma quinidine concentration after a single large oral dose, and the time of maximum concentration varied between forty-five minutes and four hours in different individuals. The rate of fall also varied

It is thus seen that unlike digitalis, which has a cumulative effect lasting days or weeks, as will be shown later, quinidine has no such prolonged effect.

In an occasional case of supraventricular paroxysmal tachycardia that does not respond to quinidine, resort may be had to *acetyl-beta-methyl-choline*, marketed under the trade name of *mecholyl.* Its effect on paroxysmal tachycardia was first described by Starr[12] This drug acts as a powerful stimulant on the parasympathetic nervous sytem, and may be effective only in supraventricular paroxysmal tachycardia. Severe toxic reactions often follow its use, such as marked flushing, nausea, vomiting, perspiration, severe asthmatic breathing and collapse Occasionally, sudden death has followed its use The most alarming symptoms occur in individuals of the vagotonic type The drug, if used at all, should therefore be given very cautiously, and atropin sulphate, $\frac{1}{50}$ of a grain, must be ready for intravenous injection immediately after the appearance of any serious symptoms

Mecholyl is given subcutaneously in dosage of 10 mg. to children, 20 mg. to young adults and 40 mg. in older adults If severe symptoms begin to appear soon after the injection, it is advisable to constrict the arm above the area of injection by an arm band to prevent rapid absorption. If the symptoms become alarming, an intravenous injection of atropin should be given at once.

In occasional cases, especially where signs of congestive failure begin to appear and the response to the other methods is poor, digitalis should be employed. This drug, however, should not be used in ventricular paroxysmal tachycardia. The manifestations of heart failure are described in Chapter XIII. The use of digitalis is described later in this chapter.

Weisberger and Feil[13] recently reported a successful response of 16 cases of persistent auricular paroxysmal tachycardia to intravenous injection

of 0 8 mg. or 4 cc. of lanatoside C, repeated if necessary in thirty minutes. All cases responded within forty minutes, the average time of response was 17.6 minutes. No toxic reaction followed

The prevention of the recurrence of attacks of paroxysmal tachycardia depends upon our ability to discover and to remove the underlying cause or causes of the attacks in the given case

Auricular Flutter

This is a form of auricular tachycardia which differs from auricular paroxysmal tachycardia described before primarily in the auricular rate The average rate here is 300 per minute with limits of slightly less than 200 and slightly more than 400 per minute.

Physiologic Mechanism: The condition is considered to be caused by a circus movement, mentioned under paroxysmal tachycardia, the wave of excitation travelling along a ring of muscle surrounding the great veins in the right auricle This excitation wave sends off continuous streams of secondary waves which spread throughout the auricular muscle The auricular contraction and relaxation therefore consist of an orderly sequential wavelike spread

Because of the rapid auricular rate, the auriculo-ventricular node has no time to recover from each impulse that reaches it The ventricles, therefore, rarely respond to all auricular impulses. In most cases there is 2:1 block, that is, there are two auricular to one ventricular contraction. Occasionally, there may be 3:1 or 4:1 block In the last two instances the ventricular rate may be within normal limits. Here, on ordinary physical examination of the heart, the auricular flutter cannot be discovered, and will be found only on electrocardiographic examination Occasionally, a mixed 2:1 to 4:1 block may occur, resulting in irregularity of the ventricular rate The mechanism is fully described elsewhere[1]

Incidence: The condition does not occur as frequently as paroxysmal tachycardia and is much rarer than auricular fibrillation. It is more frequent in males than in females and it increases in frequency as age advances. It is very rarely observed in early life.

Causes: Unlike paroxysmal tachycardia which most often occurs in the absence of organic heart disease, auricular flutter comparatively rarely occurs in normal hearts It is most often observed in such conditions as mitral stenosis, thyrotoxicosis, coronary sclerosis and hypertension The precipitating factors may be sudden heart strain, surgical operations, sudden emotional upset or sudden onset of some acute infection In some cases there is no demonstrable precipitating cause.

Subjective and Objective Manifestations The subjective manifestations may be the same as in paroxysmal tachycardia. Because flutter is more often associated with cardiac disease and because once the condition develops it is usually long lasting, cardiac failure occurs more frequently in flutter than in paroxysmal tachycardia Symptoms due to cerebral ischemia may likewise develop, especially when the ventricular rate is very rapid.

The objective manifestations are usually those of a rapid heart rate which may persist for many hours, days, weeks, months and even years with very little, if any, change from time to time Change in posture or exercise usually has no effect on the ventricular rate although the latter does occasionally accelerate the rate The rhythm is regular, but when a variable degree of auriculo-ventricular block is present, some irregularity occurs Whatever irregularity is present, however, the dominant rhythm is not as chaotic as in auricular fibrillation.

In cases where block occurs in a marked degree, the rate, as said before, may be normal, in which case the diagnosis may be made only by the electrocardiogram Thus, if the auricular rate is 300 per minute and there is 4:1 block, the ventricular rate and therefore the pulse rate will be only 75 per minute

Treatment Auricular flutter occurring as a transient manifestation requires no particular therapy. The underlying cause must be looked for and if possible removed. When the attacks are long lasting and the ventricular rate is rapid, *digitalis therapy* is called for This is particularly true if there is some evidence of cardiac failure

The physiologic effect of digitalis on auricular flutter, in most cases, is to convert the abnormal rhythm to a normal sinus mechanism. During this process, auricular fibrillation may develop which is usually transient and changes spontaneously to a normal rhythm. The mechanism of the development of transient auricular fibrillation is described under fibrillation

In some cases the effect of digitalis is to produce a varying degree of auriculo-ventricular block without interfering with the auricular flutter. This, likewise, is an effective therapeutic result, for by slowing the ventricular rate to a normal range, cardiac failure is prevented, or if present, may be relieved. In some such cases the auricular flutter may continue for some time and stop spontaneously. In occasional cases it may continue for months or even years, but if the ventricular rate is maintained at a normal level, the patient may be comfortable and able to carry on his activities unless myocardial disease is very extensive and failure, if present, continues in spite of the normal ventricular rate.

The *choice of digitalis* preparations in auricular flutter as well as any

other condition where digitalis therapy is necessary, is a matter to be decided by the physician and may have to be varied in different cases, depending upon the urgency of the case. There are a great variety of preparations on the market and it is wise to select two or three of proven value and use them consistently Shifting to different varieties from time to time at the recommendation of the pharmaceutical detail man is, in the author's opinion, practicing poor medicine In many cases, failure to obtain good results from the standard preparations is not due to the inefficacy of the drug, but to its use in insufficient dosage In others it is due to the presence of disease which interferes with the proper action of the drug, such as thyrotoxicosis, avitaminosis or severe myocardial degeneration with insufficient normal myocardium to respond In such cases, the toxic effects of the drug manifest themselves before any therapeutic value is derived In occasional cases of extreme congestive failure with marked liver and gastro-intestinal stasis, poor absorption from the gastro-intestinal tract, if the drug is given by mouth, may account for failure to obtain good results Also the retention of the drug in the fluids of massive peripheral edema may produce the same results. Lastly, digitalis preparations standing on the druggist's shelf more than two years will lose much of their potency

The usual and reliable *digitalis preparations* are those derived from the leaf of digitalis purpurea or red foxglove, first efficiently used by William Withering[11] as early as 1785 Since his day, and especially within recent years, numerous preparations have been developed in purified crystalline forms of digitalis purpurea as well as digitalis lanata, strophanthus and squill, containing glycosides related to those obtained from digitalis purpurea A few of the preparations are digitoxin, digalen, scillaren, strophanthine and ouabain Most of the preparations found on the market are no better in their effects than the standardized powdered digitalis leaf or the tincture and some are worse

The powdered leaf may be prescribed in capsule or tablet form, 1½ grains each, or in the tincture, 1 cc of which is equivalent to 1½ grains of the powder Where there is no great urgency in digitalizing the patien the drug may be administered by mouth in either of these forms in compar tively small doses, three times daily until its cumulative effect on the hea is shown It may then be continued in a small daily maintenance d to perpetuate its effect

To be specific, to effect full digitalization by the slow method, we m give two of the above sized tablets or capsules, or 2 cc. of the tincture th times a day until definite improvement is noted or signs of digitalis toxici develop Usually the full effect is produced after twelve to fou

Subjective and Objective Manifestations: The subjective manifestations may be the same as in paroxysmal tachycardia. Because flutter is more often associated with cardiac disease and because once the condition develops it is usually long lasting, cardiac failure occurs more frequently in flutter than in paroxysmal tachycardia Symptoms due to cerebral ischemia may likewise develop, especially when the ventricular rate is very rapid.

The objective manifestations are usually those of a rapid heart rate which may persist for many hours, days, weeks, months and even years with very little, if any, change from time to time. Change in posture or exercise usually has no effect on the ventricular rate although the latter does occasionally accelerate the rate. The rhythm is regular, but when a variable degree of auriculo-ventricular block is present, some irregularity occurs. Whatever irregularity is present, however, the dominant rhythm is not as chaotic as in auricular fibrillation.

In cases where block occurs in a marked degree, the rate, as said before, may be normal, in which case the diagnosis may be made only by the electrocardiogram Thus, if the auricular rate is 300 per minute and there is 4:1 block, the ventricular rate and therefore the pulse rate will be only 75 per minute

Treatment Auricular flutter occurring as a transient manifestation requires no particular therapy The underlying cause must be looked for and if possible removed. When the attacks are long lasting and the ventricular rate is rapid, *digitalis therapy* is called for. This is particularly true if there is some evidence of cardiac failure

The physiologic effect of digitalis on auricular flutter, in most cases, is to convert the abnormal rhythm to a normal sinus mechanism. During this process, auricular fibrillation may develop which is usually transient and changes spontaneously to a normal rhythm The mechanism of the development of transient auricular fibrillation is described under fibrillation

In some cases the effect of digitalis is to produce a varying degree of auriculo-ventricular block without interfering with the auricular flutter This, likewise, is an effective therapeutic result, for by slowing the ventricular rate to a normal range, cardiac failure is prevented, or if present, may be relieved. In some such cases the auricular flutter may continue for some time and stop spontaneously. In occasional cases it may continue for months or even years, but if the ventricular rate is maintained at a normal level, the patient may be comfortable and able to carry on his activities unless myocardial disease is very extensive and failure, if present, continues in spite of the normal ventricular rate.

The *choice of digitalis* preparations in auricular flutter as well as any

drug far from sufficient to produce toxic manifestations. This is true particularly when a fairly large dose of the digitalis leaf or tincture is given at one time and is less apt to occur when digitoxin is given, as said before If no therapeutic effects were produced by the given dosage which resulted in nausea and vomiting and if no cardiac signs of toxicity developed, the nausea and vomiting may be considered to be due to local gastric effect, not to intoxication The cardiac signs of toxicity may be the onset of frequent premature contractions that were not present before, marked sinus slowing, nodal rhythm, various degrees of auriculo-ventricular block and other electrocardiographic changes described elsewhere.[1]

In auricular flutter with very rapid ventricular rate and signs of failure, the rapid method of digitalization should be employed Full effects are usually shown in two to four hours if a single full digitalizing dose of digitoxin is given by mouth There is either a marked slowing of the ventricular rate or a return to a normal sinus mechanism. A maintenance dose should be continued if slowing occurs without reversion to a normal sinus rhythm If normal rhythm is restored, quinidine sulphate in maintenance doses may be employed for a week or two, as in paroxysmal tachycardia, to prevent the return of flutter

In unusually severe cases with marked left heart failure, the intravenous route may be used In such cases it is most essential to know if the patient received digitalis in large amounts within one or two weeks before Complete elimination of digitalis from the body, if the patient has been fully digitalized, may take two to three weeks, although most of the drug is eliminated within one week after full digitalization

In those cases where digitalis fails to restore a normal sinus rhythm, *quinidine sulphate* may be tried This should be given in the same dosage as in paroxysmal tachycardia This drug slows the circus movement in the auricles, thus improving the auriculo-ventricular conduction and may at times, therefore, temporarily accelerate the ventricular rate, before a normal rhythm is restored

In a small proportion of cases, neither digitalis nor quinidine will be effectual in restoring a normal rhythm In such cases the ventricular rate should be kept low by digitalis, and we must watch for signs of failure. If failure develops, treatment should be instituted as described in Chapter XIII

Auricular Fibrillation

Auricular fibrillation, next to ectopic beats, is one of the commonest arrhythmias It is characterized clinically by a total irregularity of the ventricular beats

Physiologic Mechanism The condition is considered to be due to a

circus movement, as in auricular flutter, but with a shorter path of the ring and faster conduction of the impulse The greater rapidity of the spread of the impulse, not giving various parts of the auricle enough time to recover from previous contractions, results in a great deal of interference with its spread in various parts of the auricular musculature The auricular contraction is therefore very rapid and extremely uneven or chaotic The rate of travel of the auricular wave, as measured in the electrocardiogram, is over 400 times per minute and may reach 600 or more per minute in some cases.

As a result of this rapid and irregular propagation of the impulses in the auricles, the auriculo-ventricular node is stimulated at a rapid and irregular rate of speed. Due to a considerable amount of natural refractoriness of this node as well as to the fact that some of the impulses do not reach it or are too weak to pass through the auriculo-ventricular node, only a certain number of the auricular impulses pass to the ventricles The number varies in different cases This results in a rapid and irregular ventricular contraction The ventricular rate in untreated cases may, in some instances, be as high as 200 or more, although in most cases it is less The rate may be greatly diminished and brought down to a normal or subnormal level by producing a certain degree of block in the auriculo-ventricular node by digitalis

Fundamentally, then, auricular fibrillation has the same mechanism as flutter, except for a more rapid rate of travel of the impulses which results in interference in conduction in the auricles In fact, one may often be transferred into the other spontaneously or by drugs or through vagal effect Thus, as indicated before, digitalis may convert flutter into fibrillation before a normal sinus mechanism is re-established. This is accomplished mainly by an increase in the rate and shortening of the course of the circus movement At the same time there is a decrease in the refractory period of the muscle through its effect on the vagus, although its direct effect on the muscle is to increase the refractory period Quinidine, on the other hand, may convert auricular fibrillation into flutter. This is accomplished by increasing the refractory period of the auricular muscle and increasing the length of the circuit This is helped by the depressing effect of quinidine on the vagus.

Recently, Prinzmetal and co-workers[19] have shown that premature contractions, auricular tachycardia, flutter and fibrillation have the same mechanism of an ectopic focus of impulse formation This impulse spreads in all directions rather than in a circus as originally postulated by Lewis. The differences of the various arrythmias are dependent upon the rapidity of formation of this ectopic impulse. The circus movement theory is thus disproved.

Causes Auricular fibrillation is caused by the same conditions as auricular flutter A more advanced disturbance it is oftener associated with organic heart disease, although it is observed occasionally in cases showing no structural cardiac disease The author has under observation a male 21 years old, with no demonstrable organic heart disease, who gets recurring attacks of auricular fibrillation after any marked excitement. Quinidine sulphate restores a normal sinus mechanism within a few hours after the onset of the attack In another male 28 years old, also having no organic heart disease, the attacks occur spontaneously without any demonstrable exciting cause, and stop spontaneously after three to ten days He does not respond to quinidine

The underlying pathologic changes which bring about this arrhythmia are probably those which interfere with a proper blood supply to the auricular muscle together with vagal irritation, as recently shown experimentally by Smith and Wilson[16] Any toxic state, particularly thyrotoxicosis, as well as extreme nervous shock may also produce an attack We[17] reported an example of transient auricular fibrillation lasting one day in a healthy young male, following electric shock

Subjective and Objective Manifestations Where the condition appears as a transient manifestation, the patient may experience the same abnormal sensations during the attack as in paroxysmal tachycardia or in flutter. As the condition becomes chronic, there may not be any abnormal sensations due to the arrhythmia itself, especially when the ventricular rate is controlled by digitalis or by inherent auriculo-ventricular block. Inasmuch as the arrhythmia, if uncontrolled, is apt to precipitate congestive failure, symptoms due to failure will ensue in addition to those disturbances that may be caused by the arrhythmia itself

The objective findings consist of a complete irregularity of the apex beat and the pulse rate The time interval between any two apex beats and the character and intensity of the first and second heart sounds vary from moment to moment The first heart sound appearing after a comparatively long diastolic interval may be of normal intensity and character That appearing after a very short diastolic period is usually louder than normal In some heart beats which follow extremely short diastolic intervals the second heart sound may not be heard at all or may be almost inaudible This depends upon the degree of ventricular filling If the ventricles did not fill sufficiently during the diastolic period to raise its pressure high enough to open the semilunar valves, no second heart sound will be heard If the degree of filling of the ventricles was sufficient to open these valves but not enough to raise the arterial pressure to a high enough level, the second sound will be of poor quality

tensity will vary from time to time. Systolic murmurs will be heard best during those beats which follow long diastolic intervals. Also a diastolic murmur will be heard best during a long diastole, while during a short diastole it may be hardly audible or may not be heard at all.

The pulse will exhibit a marked irregularity in rhythm, and variability in rate and amplitude. This is caused by the variations in the rate and rhythm of the cardiac contractions and in the amount of blood discharged [illegible] rring after a [illegible] If the dis- [illegible] ill be small [illegible] Those heart contractions which are ineffective in opening the semilunar valves will of course produce no pulse. For this reason there is always a so-called "pulse deficit" in this condition That is, the number of apex beats per minute is always greater in this arrhythmia than the pulse rate. This pulse deficit is greatest when the ventricular rate is very high, and becomes less as the ventricular rate slows When the ventricular rate becomes very slow, there may be no pulse deficit at all The reason is very simple With a slower ventricular rate there is more time during diastole to fill the ventricles effectively and there is, therefore, an expulsion of a sufficient amount of blood into the arterial system during each ventricular contraction

The disturbances in the heartbeat and in the pulse are often further complicated by the occurrence in some cases of ventricular premature contractions They occur particularly in overdigitalization when the ventricular rate becomes very slow In such cases, pulsus bigeminus usually develops.

The blood pressure in auricular fibrillation varies and corresponds to the quality of the pulse The variation may be as high as 20 or more millimeters between the maximum and minimum systolic and a little less between the maximum and minimum diastolic pressure

Prognosis: Auricular fibrillation may be transient and unimportant Most often it becomes permanently fixed and chronic In such cases it often helps break down the cardiac reserve and brings about congestive failure. This may occur especially when the ventricular rate is not controlled or is not controllable by digitalis In the majority of cases the rate is slowed by digitalis if given in sufficient doses

In addition to congestive failure, the arrhythmia often predisposes to the formation of mural thrombi *in the auricles which serve as embolization, to* be described in a later chapter

Treatment. Where auricular fibrillation is intermittent, appearing and disappearing spontaneously without any definitely known reason, the attacks may frequently be aborted and prevented from recurring by *quinidine.* The method of its administration is the same as in paroxysmal tachycardia.

ı chronic and continuous auricular fibrillation where the ventricular is within normal limits, no particular drug therapy is necessary unless iac failure is present, and this, when it occurs, should be treated as ribed in Chapter XIII. In a few such cases, with or without failure, rhythm occasionally reverts spontaneously to a normal sinus mechaı and back again to fibrillation These may be benefited by quinidine. ; drug should never be used where the arrhythmia is chronic and per-:nt, associated with mitral stenosis or other organic heart disease If ormal rhythm is restored in such cases by the drug, reversion to the ormal rhythm will almost invariably occur. Furthermore, the poten-ty for embolization or cardiac asystole is always present if fibrillation ddenly abolished by the drug. In an unusually rare case of persistent cular fibrillation with a slow ventricular rate and with extreme, irreduc- congestive failure quinidine may restore a normal sinus mechanism and ı the condition In such hopeless cases the drug may be tried as a last rt

ı the vast majority of cases of auricular fibrillation, *digitalis* is the drug hoice The main physiologic effect of this drug in this arrhythmia is to duce a varying degree of auriculo-ventricular block, partly by its stimung effect on the vagus and partly by its direct effect on the auriculo-tricular conduction system As a result of such block, many of the icular impulses can not pass to the ventricles. The ventricular rate is s slowed. Only the more effective auricular impulses result in ventricu- response. Because of the slowing effect on the ventricles, the filling l emptying of these chambers are more complete so that the arterial tem is filled more effectively. The pulse becomes slower and of better ility, although the arrhythmia persists The pulse deficit is greatly inished and may often be entirely eliminated when the ventricular rate educed to 80 or less per minute.

ın example of the progressive decrease in the pulse deficit in a patient h auricular fibrillation who was fully digitalized by fourteen tablets, 1½ ins each of the digitalis leaf, by the slow method over a period of three 's is shown in Figure 48 It will be seen that the greatest pulse deficit urs before digitalis therapy is started This is due to the fact that ny heart beats are ineffective in sending out a sufficient volume of blood produce a palpable radial pulse With considerable slowing of the ven-:ular rate at the end of the first day, the pulse, likewise, slows but not in same degree, so that the pulse deficit is greatly reduced. At the end of second day there is further reduction in the ventricular rate as well as the pulse rate, the latter further lagging, so that the pulse deficit is now rkedly reduced At the end of the third day the ventricular rate is uced to the lower normal limits All ventricular beats are now effective

in filling the arterial system so that the pulse rate is the same as the ventricular rate, that is, the pulse deficit disappears.

The method of digitalization in auricular fibrillation is the same as in auricular flutter If the ventricular rate is extremely fast and signs of congestive failure begin to appear, the rapid method is to be employed either by mouth or intravenous routes The same precautions are to be used as in auricular flutter. If the ventricular rate is not excessively rapid, or if rapid is not associated with any signs of congestive failure, the slow and safer method is to be employed In either case, the effect of the drug

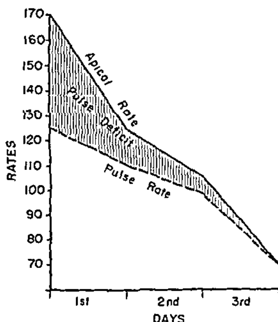


Fig 48—The Effect of Slow Digitalization, over a Period of Three Days, in a Case of Auricular Fibrillation There is a progressive diminution in the heart rate, pulse rate and pulse deficit See text

is to be perpetuated by a daily maintenance dose as long as the arrhythmia persists.

Ventricular Fibrillation

The diagnosis of this arrhythmia can only be made by the electrocardiogram. This arrhythmia may occur as a transient or as a terminal manifestation of heart disease or of grave infections, and is fully described elsewhere.[1] In the transient form the condition may produce syncope and convulsions as in ventricular asystole, due to auriculo-ventricular block, or in cardiac asystole due to sino-auricular standstill, as described in

Chapter XV. The transient form may recur with temporary spontaneous recovery. Quinidine may perhaps be of some value, although questionable The management of this disturbance during operation is discussed in Chapter XXXI.

Bradycardia and Arrhythmia due to Auriculo-Ventricular Conduction Disturbances

Interference with the conduction of the impulse in its passage from the auricles to the ventricles produces the condition known as auriculo-ventricular heart block Local interference with conduction in the bundle branches produces intraventricular or bundle branch block Inasmuch as bundle branch block itself does not produce bradycardia or arrhythmia, except when the conduction in both branches is evenly interfered with, we shall leave it out of consideration here.

Auriculo-Ventricular Heart Block

Physiologic Disturbances This condition is caused by defective conduction in the auriculo-ventricular node or the bundle The disturbance in conduction may be temporary or permanent and partial or complete.

In partial block there may merely be a delay in the passage of the impulse, or there may be an occasional complete interference with its passage In complete block, none of the auricular impulses can pass to the ventricles, and a new center is established below the area of block where ventricular impulses develop If the new center develops slowly, ventricular asystole for a variable period of time will result

Causes Heart block may be caused by structural disease of the heart due to arteriosclerosis, various infectious diseases, particularly rheumatic fever and diphtheria, and some congenital defects In milder grades it may be caused by excessive vagal activity, and may be temporarily produced by the carotid sinus reflex It is questionable, however, if vagal stimulation alone will produce a sufficient degree of block There is usually some structural disease present in addition. It may also be produced by certain drugs particularly digitalis In such cases its effect is mainly through its action on the vagus. Here again the higher grades of block are much more frequently produced by the drug in the presence of organic heart disease

There are cases of heart block on record where no structural disease of the conduction apparatus has been found on postmortem examination. In such cases the condition was probably due to functional disturbances, temporary ischemia or to some intoxication affecting the lower conduction apparatus during life

Subjective and Objective Manifestation: These depend mainly upon the degree of block and the sensitivity of the individual

In the first grade, where there is mere delay in the auriculo-ventricular conduction time, the patient may have no disturbances other than those caused by the underlying disease There are also no abnormal physical findings except where the delay is very marked when careful inspection of the venous pulse in the neck, if present, may reveal a prolonged interval between the auricular and ventricular waves The condition, however, may be recognized by a prolonged a-c interval in the phlebogram, or, easier, by a prolonged P-R interval in the electrocardiogram

In the second grade, where some ventricular beats are dropped out, the patient may complain of the same disturbances as those caused by premature contractions which occur very early in diastole The greater the number of dropped ventricular beats the greater the disturbance the patient may experience *The clinical differentiation* between premature contractions and dropped ventricular beats caused by block can be made by palpation of the pulse and by listening to the heart sounds In an early premature contraction which yields no pulse, there is at least one heart sound heard In dropped ventricular beats, no heart sounds are heard during the pause.

In the third grade of heart block, where there is a complete interference with conduction between the auricles and ventricles, the clinical manifestations vary with the suddenness of onset of the condition, the rapidity of the development of the new idioventricular rhythm center, and the functional capacity of that center. The condition is fully described in Chapter XV.

In many cases before complete block is permanently established, the degree of block may change from partial to complete and back to partial, so that whatever disturbances are present from time to time, may vary in degree.

When permanent complete block is established with a ventricular rate of 20 beats or more per minute, the patient may, in some cases, be quite comfortable and may even be able to engage in some activity The degree of disability in such cases will depend more upon the condition of the myocardium and the general constitutional state than on the block The author has had several cases of arteriosclerotic heart disease with complete auriculo-ventricular block and a ventricular rate no higher than 30 beats per minute who were quite comfortable and able to engage in a fair amount of activity. Cases where the heart rates are higher, especially in congenital heart block, the condition is much more compatible with a normal existence The author has under observation, a girl, 25 years of age, with congenital heart block and a ventricular rate of 45 beats per minute who works as a clerk in a store and often goes out to dances with apparently no ill effects.

The relative comfort of these patients can be explained by the fact that although the ventricular rate is slow, the minute volume output of blood under average conditions may be normal. This is due to the fact that because of the longer ventricular diastole, there is greater filling of the ventricles and therefore the stroke volume is correspondingly greater than in normal individuals. Thus, a normal stroke volume, say of 2 ounces, with a rate of 80 beats per minute, will result in a minute volume output of 160 ounces. In complete heart block with a rate, say, of 20 beats per minute, and a stroke volume of eight ounces, the minute volume output will likewise be 160 ounces. In the course of time, however, the excessive stretching and tension of the ventricular wall resulting from overfilling will produce failure. This is more apt to occur early if there is marked disease of the ventricular musculature. The adaptation to work is likewise very poor in cases of complete heart block, since very little, if any, acceleration of the ventricular rate occurs under strain or excitement.

The physical findings of complete heart block vary. During complete asystole, no apex beat is detectable and no ventricular heart sounds are heard. Often, however, auricular sounds may be heard. They are very weak and distant. No pulsation is felt over any of the peripheral vessels, and of course, no blood pressure readings can be obtained. With resumption of ventricular contractions, the ventricular heart sounds become audible at a slow rate, and the auricular sounds may also be perceptible at a faster rate. Some of the auricular contractions which are close to the ventricular contractions will accentuate the ventricular first sound, as will be described in Chapter VIII.

volume of blood entering the arterial system during systole. The low diastolic is due to greater emptying of the blood from the arteries into the capillary system during the long diastolic interval.

Treatment: The treatment of partial auriculo-ventricular block consists of proper management of the underlying condition which causes such block. No particular specific drug therapy is necessary for the block itself. If digitalis is the underlying cause in any case it should be discontinued, unless there is marked congestive failure, when it should be used very cautiously. If quinidine is the cause, it should also be discontinued, or used under careful supervision if absolutely essential

Complete heart block, without the Adams-Stokes syndrome, requires no specific therapy In fact, there is no drug that effectually influences the block itself. Congestive failure, if present, should receive appropriate therapy, as should the anginal syndrome when it occurs. These will be discussed in Chapters XIII and XIV.

If the Adams-Stokes syndrome develops, urgent therapy is called for, to be discussed in Chapter XV

REFERENCES

[1] Sigler, L H The Electrocardiogram, Its Interpretation and Clinical Application New York, Grune & Stratton, 1944 Pages 74–181

[2] Struthers, R R, and Bacal, H L Determination of the activity of rheumatic infection in childhood Canad M A. J. 29 470, 1933

[3] Sigler, L H Electrocardiographic observations on the carotid sinus reflex Am Heart J 9 782, 1934, Further observations on the carotid sinus reflex Ann Int Med. 9 1380, 1936

[4] —— H[illegible]

[5] —— [illegible] coror[illegible] sinus reflex as an aid in the diagnosis of coronary disease, its value compared with that of the electrocardiogram New England J Med 226 46, 1942

[6] Mackenzie, Sir James Disease of the Heart London, Oxford Publication, 1918

[7] Kline, E M, and Bidder, T G A study of the subjective sensations associated with extrasystoles Am Heart J 31 254, 1946

[8] Barker, P S, Wilson, F N, and Johnston, F D The mechanism of auricular paroxysmal tachycardia Am Heart J 26 435, 1943

[9] Evans, W The unity of paroxysmal tachycardia and auricular flutter Brit Heart J 6 221, 1944

[10] Weisman, S A Studies on the time required for the elimination of quinidine from the heart and other organs Am Heart J 20 21, 1940

[11] Delevett, A F, and Poindexter, C A Plasma concentrations of quinidine with particular reference to therapeutically effective levels in two cases of paroxysmal nodal tachycardia Am Heart J 32 697, 1946

[12] Starr, I Acetyl-B-methylcholine III Its action in paroxysmal tachycardia and peripheral vascular disease with a discussion of its action in other conditions Am J M Sc 186 330, 1933

[13] Weisberger, A S, and Feil, H Lanatoside C in the treatments of persistent paroxysmal auricular tachycardia Am Heart J 34 871, 1947

[14] Withering, W An Account of the Foxglove and Some of its Medical Uses, with Practical Remarks on Dropsy and Other Diseases Birmingham, England, 1785

[15] Gold, H, Kwit, N T, Cattell, McK, and Travell, J Studies on purified digitalis glucosides. IV The single dose method of digitalization. J A M A 119 928, 1942

[16] Smith, J R, and Wilson, K S Studies on the production and maintainance of experimental auricular fibrillation Am Heart J 27 176, 1944

[17] Sigler, L H, and Schneider, J J Electrocardiographic changes in a case of shock Am Heart J 12 236, 1936

[18] Prinzmetal, M, Sellers, A L, Corday, E, Flieg, W, and Kruger, H F The mechanism of the auricular arrhythmias Unpublished Personal communication with the author

CHAPTER VIII

Heart Sounds: Normal and Abnormal

THE HEMODYNAMIC action of the heart and the closure of its various valves produce sound vibrations which are propagated to the surface of the chest. Here, they can be picked up and transmitted to the ear by auscultation or recorded by suitable sound recording apparatus, the phonocardiograph.

The sound vibrations produced have certain intensities and frequencies of oscillation. According to Rappaport and Sprague,[1] the oscillatory frequency band of the heart sounds and murmurs is below 1,000 cycles per second. The portion which is within auditory perception, ranges between 60 to 400 cycles per second.

Inasmuch as sound vibrations traveling through media of various densities, such as the chest tissues, undergo a certain degree of distortion and attenuation, much of the sound produced in the heart does not reach the surface of the chest. Furthermore, those regions of the chest which are closest to the heart and great vessels receive the maximum amount of sound energy. Hence, heart sounds are heard better over some parts of the chest than others, and in many parts, they are normally not heard at all. There is also the probability that some of the sound vibrations produced in the heart cannot be heard even if they reach the surface of the chest because the human ear cannot be excited by vibrations beyond the oscillatory frequencies given above. This is more true with some individuals than others, for there is a variation in the auditory acuity and in training of different people in the perception of sound.

AUSCULTATION

The sound reaching the surface of the chest may be perceived by placing the ear on the chest—immediate auscultation—or, by means of a suitable stethoscope—mediate auscultation. The former method has been abandoned because the sound perceived is diffuse, ill-defined and of poor quality. The method may be used, however, in listening to the lungs.

Mediate Auscultation Stethoscopy: The stethoscope has undergone marked modification and improvement since its original introduction in a very crude, solid form by Laenec in 1819. The usual, binaural stethoscope used in practice at present consists of two rubber tubings leading to ear pieces from a receiver or chest piece. The chest piece is either an open bell or a flattened bell air chamber covered by a diaphragm, known as

"phonendoscope," as the Bowles type Some stethoscopes have a combination of both and can be switched from one to the other.

The difference between the open bell and diaphragm type of chest piece is that the latter filters out some of the low frequency sound vibrations which ordinarily drown a portion of the high pitched sound waves. This accentuates the faint, high pitched and barely audible sound. For this reason, the diaphragm type of stethoscope is preferable to the open bell type for the detection of a high pitch diastolic murmur, as in aortic insufficiency. On the other hand, the open bell is preferable to the diaphragm type for the detection of a low pitch murmur as the diastolic murmur of mitral stenosis.

As a matter of fact, the open bell may also be considered a diaphragm type of chest piece The skin forms a diaphragm when the chest piece is applied to it and the fleshy subcutaneous portion acts as a damping medium By exerting pressure on the bell, there is an increase in the natural period of the area of skin surrounded by the rim, thus attenuating the low frequency components The amount of pressure necessary to produce this effect, however, may discomfort the patient.

In selecting any chest piece, it is essential that its internal volume be as small as possible, for the smaller the volume, the greater the variation in the air pressure and, therefore, the greater the intensity of sound. This is true also of the tubing, which is to be as short as possible If the diaphragm chest piece is used, the diaphragm should be made of very thin plastic, not metal, to prevent a metalic ring to the sound.

The Normal Heart Sounds

By normal heart sounds, we mean sounds ordinarily heard over given areas of the precordium in normal individuals with no organic cardiovascular disease It must be understood, however, that such sounds do not necessarily always indicate a normal heart. Many cases with organic heart disease may have normal sounds as judged by our standards of normality. On the other hand, in many normal individuals, the heart sounds may deviate from the normal and present some unusual characteristics. Normal sounds and some of their abnormalities must, therefore, not be the only criteria in the diagnosis of heart disease

The normal audible heart sounds are ordinarily two in number, designated as first and second Occasionally, a third heart sound may be heard between the lower sternum and apex, especially when the patient is in the dorsal, or better, in the left lateral recumbent posture.

The first heart sound is the longest of the three. It occurs during the isometric and the very early part of the ejection phases of ventricular contraction, at the moment and immediately after the closure of the auriculo-

ventricular valves and the opening of the semilunar valves It varies somewhat in length with the heart rate. With a rate of 72 to 80 beats per minute, its approximate duration is 0 10 second and it becomes slightly shorter as the rate goes up. It is heard loudest at the apex and is of deep pitch and of a more or less booming quality. It usually appears to be single and homogeneous. However, in reality it is a complex sound, made up of many components

The mechanism of its production has not as yet been fully established Some consider it to be due to a combination of muscular contraction and closure of the auriculo-ventricular valves. This has been disputed by others Lewis and Dock[2] believe that it is produced by sudden tension of the auriculo-ventricular valve leaflets during their closure. They show that the rubbery mass of heart muscle gives off no sound. Wiggers[3] attributes the sound to sudden elevation of intraventricular pressure due to ventricular contraction which produces vibrations of the auriculo-ventricular valves, chordae tendineae and walls of the ventricles Wolferth and Margolies[4] believe that the speed of development or gradient of rise in intraventricular pressure in each ventricle and its effect of setting ventricular structures into vibration governs the production of the sound and the magnitude of its vibration or loudness. In some cases, the sudden impact of the contracting apex against the chest wall may be a contributing factor in the production of this sound Orias and Braun-Menendez[5] believe that the first sound is caused by the following four factors: the residual vibrations of auricular contraction, the tension of the ventricular muscle; the closure of the auriculo-ventricular valves; and the opening of the semilunar valves with the movement of blood into the central arteries in the early ejection phase.

The second heart sound is shorter than the first and is of higher pitch and snapping quality. It is usually heard best at the second interspace just to the right and left of the sternal border, designated by the terms *aortic* and *pulmonic areas* respectively These, of course, are not the actual locations of the aortic and pulmonic valves, as shown in Figure 49 They are merely areas on the chest where the arterial trunks propagating the sound vibrations are closest to the chest wall In some cases, the second, like the first sound, is heard best at the apex. The duration of the second sound is about 0 07 second, with a heart rate of 72 to 80 beats per minute and shortens slightly with increase in rate.

The second sound is caused by the sudden simultaneous closure of the aortic and pulmonic semilunar valves at the end of systole, when the intrapulmonic and intra-aortic pressure rises above the intraventricular pressure

Normally, the second sound is homogeneous Its intensity, at the aortic

and pulmonic areas, usually varies at different ages. In early life, up to about 20 years of age, the pulmonic second sound is of greater intensity than the aortic. Between about 20 to 40 years of age, the sounds are of

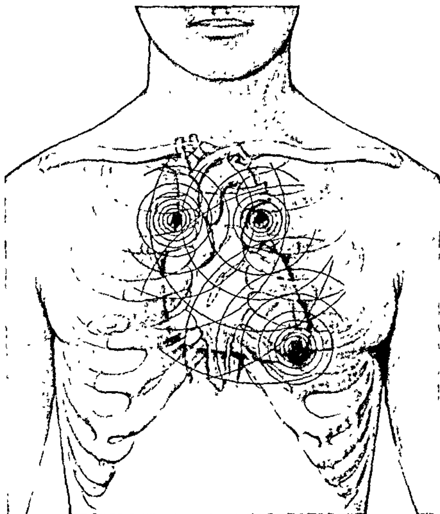


FIG 49.—AREAS OF MAXIMUM INTENSITY AND TRANSMISSION OF THE HEART SOUNDS AND THEIR RELATION TO THE VALVULAR ORIFICES The loudness of a given sound in any region of the precordium is represented by the density of the sound waves A, aortic second sound, P, pulmonic second sound, F, first sound For description, see text.

about equal intensity at both areas Above 40 years of age, the aortic second sound is more intense than the pulmonic. The greater intensity of the aortic second sound with advancing age is due to gradual development

of aortic sclerosis which increases the intra-aortic blood pressure. The accentuation of the aortic second sound is most pronounced in the presence of systemic arterial hypertension.

The third heart sound, when present, is usually very feeble and is much shorter than either of the other two. Its duration is approximately 0.04 second or less. It is probably caused by the inrush of blood in the ventricles soon after the auriculo-ventricular valves open in early diastole. It is heard best at the apex or between the apex and left lower sternal border with the patient lying in the left lateral position.

Variations in the Heart Sounds: Normal and Abnormal

The heart sounds may vary in their character under normal and abnormal constitutional states and in the presence of organic heart disease. To ascribe pathologic significance to heart sounds, we must therefore have some knowledge of these variations and their mechanism.

The variations in the heart sounds may consist of an increase or a decrease in their intensity, splitting or reduplication, gallop rhythm and the occurrence of snaps, clicks, squeaks, splashes and so on.

Increase in intensity of the first and second sounds and occasionally also in the third may occur after exercise, excitement, in nervous and emotional states and when the metabolic activity of the body is abnormally increased as in thyrotoxicosis and fever Also, in systemic hypertension the first sound and particularly so the aortic second sound are accentuated, the latter often assuming a ringing quality. In intrapulmonic hypertension, the pulmonic second sound is accentuated.

Increased intensity of the heart sounds in these constitutional states are not due to disease of the heart but to the increased gradient of intraventricular pressure, producing more rapid vibrations of its various components, as well as to tenseness of the valves in the process of closure. In the course of time, if the abnormal constitutional state persists, the heart undergoes hypertrophy which is, of course, the result, not the cause, of the abnormal state

Some forms of heart disease are often associated with increased intensity of the heart sounds Thus, in mitral stenosis, there is usually an accentuation of the first, the pulmonic second and occasionally also of the third sound In some cases an accentuated third sound is as valuable a sign in this disease as the diastolic murmur It is spoken of as the "opening snap" of mitral stenosis It has a sharp clicking or snapping character, occurring shortly after the second sound. The first sound is often accentuated also in paroxysmal tachycardia. In aortic sclerosis and in luetic aortitis the aortic second sound is frequently accentuated even in the absence of hypertension

Decreased intensity of the first and second sounds may occur on changes in

posture such as in assuming the dorsal, recumbent position, when the heart and great vessels move away a slight distance from the anterior chest wall. The sounds are also diminished in intensity in individuals with thick chests and large breasts and in pathologic conditions of the chest such as pleural effusion, emphysema and pneumothorax In peripheral circulatory failure due to shock induced by long illness, trauma, exhaustion and toxic states, the sounds may become very weak due to insufficient filling and emptying of the heart. The subject of shock is fully discussed in Chapter XVI

In the absence of the above conditions, marked diminution in the intensity of the first sound at the apex is highly suggestive of myocardial disease and failure, especially so, when the quality of the sound is impure or mixed with a systolic murmur Usually, the second sound appears to be relatively accentuated in such a condition and if the heart rate is rapid, a characteristic "tic-tac" quality appears. It must be remembered, however, that occasionally we may find marked diminution in the intensity of the first sound or of both sounds in a perfectly normal individual Diminished intensity of the aortic second sound is often observed in aortic stenosis and insufficiency, and of the pulmonic second sound in pulmonic stenosis and insufficiency

Reduplication of the first sound consists of splitting of the complex components of that sound in two distinct portions without an appreciable interval between these portions. The mechanism of its production is not entirely clear. Wolferth and Margolies[6] believe that it is due to some asynchronism in contraction of the right and left ventricles which exists in some degree even in normal hearts Orias and Braun-Menendez[5] have shown by simultaneous phlebographic and phenocardiographic studies that splitting of this sound is merely an exaggeration of the separate sounds induced during the isometric and early ejection phases of ventricular contraction which normally produce the more or less homogeneous first sound

The condition may occur in normal individuals In some young people, the intensity and duration of the first sound as well as its splitting may appear and disappear in various phases of respiration Lewis[7] has found a reduplication of the first sound in young individuals under strain. He demonstrated it to be due to temporary dilatation of the right ventricle

A reduplicated first sound may exhibit itself in some cases in the form of a normal first sound followed by a click which in its time relationship corresponds to the opening of the semilunar valves In some cases, this click-like sound may occur together with a split first sound

Reduplication of the second sound may occur at the aortic area in systemic hypertension and in the pulmonic area in intrapulmonic hypertension. It may also often be observed in perfectly normal individuals, due perhaps to slight differences in the time relationship of the closure of the aortic and pulmonic valves.

In the presence of some forms of heart disease, reduplication of the heart sounds occurs frequently. Thus, in mitral stenosis, the first and pulmonic second sounds are often reduplicated. Delayed auriculo-ventricular conduction may occasionally produce slight reduplication of the first sound. Bundle branch block frequently produces reduplication of the first and second sounds This is due to an earlier contraction of one ventricle than the other and therefore to an earlier closure of the auriculo-ventricular and semilunar valves on one side than on the other. In this condition, there is also a marked diminution in the intensity of the first sound, and often also a palpable reduplication of the apex beat

Gallop Rhythm: This is one of the most important abnormalities of heart sounds which, in its true form, designates the presence of grave myocardial disease with actual or impending congestive failure It is characterized by a triple sound resembling that of a galloping horse, from which the term is derived. In reality, it consists, however, merely of the ordinary sounds in modified forms. Thus, the first sound is usually very weak, at times hardly audible, the second sound louder, especially so at the pulmonic area and the third sound is usually as loud and even louder than the second.

The third sound in this condition, occupies a variable position in diastole In most cases, it follows immediately the second sound, a condition spoken of as a *protodiastolic gallop* These variations in location are very difficult or impossible to determine by auscultation if the heart rate is rapid.

A gallop rhythm is heard best at the apex or along the left sternal border in the fourth left interspace. Occasionally, it is heard in the midsternal region or at the base In some cases, it may be heard over the whole precordium It is usually most pronounced in the recumbent posture, and may at times be evanescent

The physiologic mechanism of a gallop rhythm has not as yet been definitely established The background is marked myocardial disease and dilatation of one or the other or both of the ventricles This is associated with overfilling of the given ventricle and a much higher than normal intraventricular pressure during diastole, inasmuch as not all the blood is expelled during systole The left ventricle is the one most often affected early or more affected than the right ventricle, as shown by the presence of signs of pulmonary stasis in most of the cases. Of course, the right ventricle also fails sooner or later Ventricular failure results in an increased intra-auricular pressure

These intracardiac pressure changes and the insufficient contractile force of the heart muscle under the added strain are undoubtedly the causes of the modification of the heart sounds which constitute a gallop rhythm. The third sound in the *presystolic gallop*, occurring in its time relationship during auricular systole, that is, near the end of ventricular diastole, probably represents an attempt to expel the blood remaining in the auricles

into the overfilled ventricles. This remaining auricular blood has to pass through a comparatively narrow slit between the compressed auriculo-ventricular valves due to increased intraventricular pressure, a condition somewhat equivalent to organic mitral stenosis. The vibrations thus set up, which normally merge with events of early ventricular contractions into a homogeneous first sound, are now separated into two distinct sounds.

The third sound in *protodiastolic gallop* rhythm is most likely a modified normal third heart sound, for it corresponds in its time relationship to that sound. As such, it occurs during the period of maximum flow of blood from the auricles into the ventricles in the early diastolic filling of the ventricles Its accentuated character is probably due to a greater auricular volume being expelled into the dilated and partly filled ventricular chambers because of improper emptying during the previous ventricular systole.

The *mesodiastolic gallop* is considered to be a "summation gallop." As a result of a rapid heart rate, the events responsible for the presystolic and protodiastolic rhythms merge together. It may also occur in cases where the heart rate is not excessively rapid but where there is a prolonged auriculo-ventricular conduction time.

Sounds Simulating Gallop Rhythm: It is very essential to differentiate a gallop rhythm from the other sounds which may simulate it, in view of the serious prognostic significance of the former

One of these is the triple sound caused by an accentuated physiologic third sound, occasionally heard in young normal individuals or in thyrotoxicosis and in nervous and emotional states. The three sounds here are usually greatly accentuated and the heart is markedly hyperactive, as determined by the impulse beat and fluoroscopically. There is also no detectable evidence of myocardial insufficiency.

Another condition is a delay in the auriculo-ventricular conduction time. Here, the pathologic condition may be strictly localized in many cases, carrying no serious prognosis. Because of the delay in the conduction, the auricles will contract long before the ventricles and the accentuated inflow wave thus set up will produce sound vibrations which are separated from the first sound.

A third is bundle branch block which, in itself, may occasionally not be very serious Here, the triple sound is due to splitting of the first sound followed by the second sound. In fact, a quadruple sound may, at times, be heard in such cases due to splitting of the first and the second sounds.

A fourth is calcification of the pericardium, described by Lian and co-workers.[8] The condition is very rare. The third sound here is of higher pitch and louder than in gallop rhythm and is synchronous with a vigorous apex impulse.

Systolic Gallop Rhythm. This is rather rare It has been observed in occasional cases of hypertension, aortic insufficiency and in subacute febrile states. It is characterized by a triple sound, the first two occurring during systole It must be differentiated from a split first sound It is heard best at the aortic area and is probably caused by the impact of the aorta against the surrounding structures during its early systolic expansion

Auricular Sounds. These can be best elicited in complete heart block. If the heart is carefully auscultated in such cases, very faint sounds are heard between the less frequent ventricular sounds The characteristic of these sounds is that those produced by the auricular contractions occurring very close to or actually superimposed on a ventricular contraction are louder. For this reason, it is believed that the auricular sounds are actually produced by events in the ventricles, induced by a greater forward propulsion of blood during auricular systole and not by the contraction of the auricular muscle Each time the auricles contract during the long diastolic period, there is a sudden inrush of blood in the partially filled ventricles, producing sound vibrations The auricular contraction occurring close to the ventricular finds the ventricles more filled and there is therefore greater intraventricular tension associated with closure of the auriculoventricular valves

Abnormal Sounds Produced by Extrinsic Factors. In various abnormal states of the structures or organs adjacent to the heart, such as in marked gaseous distention of the stomach and colon and in pneumothorax, peculiar knocking sounds may be heard during systole and diastole. Recently, Hamman[8] described cracking, crepitating, bubbling, clinking and popping sounds in cases of emphysema of the mediastinum which probably originate from interstitial emphysema of the lungs

Phonocardiography

The graphic method of study of the heart sounds has some advantages over the auscultatory method In the first place, it yields a permanent record of the given sounds and can thus be more definitely compared with any future alterations that may occur as a result of disease Secondly, we get a visual picture of all the vibratory portions of each sound, not merely the audible parts Thirdly, it eliminates the element of individual variations in auditory perception of different examiners so that a record of a given case will look the same to all observers. It has the disadvantages, however, of requiring training and experience in its recording and interpretation and in being time-consuming

The principle of phonocardiography is the same as that of auscultation.

The sound vibrations are transmitted to a resonator, the movements of which are recorded. In the case of auscultation, the resonator is the tympanum of the ear and the recording is done by our auditory perception In phonocardiography, the resonator is an artificial membrane, the movements of which are recorded either directly, by means of a suitable apparatus, or indirectly by transforming such movements into electric currents

The indirect method is the one employed in present day phonocardiography. The sounds are transmitted to a microphone disc, the delicate diaphragm of which acts as a resonator which produce alternations in the current of an electric circuit These are recordable either by a string galvanometer or by a less sensitive oscillograph In the latter case, the electrical vibrations are first amplified by vacuum tubes.

Complete historical reviews of the development of the study of heart sounds by various authors may be found in the monograph by Orias and Braun-Menendez[5] and in the paper by Bierring, Bone and Lockhart.[10] The description and the mode of operation of any given apparatus may be obtained from the manufacturer.

In registering the heart sound it is essential to eliminate all extrinsic sounds and noises in the room, and those caused by friction of the microphone on the chest caused by respiratory movements and by rubbing the microphone by an assistant's fingers

Phonocardiographic Tracings In all tracings, two distinct groups of vibrations are observed representing the first and second sounds. In some cases, a third group is noted soon after the second group, representing the third heart sound and one or two short vibrations occur immediately before the first group, representing auricular contractions In a study of 151 normal males, Boyer, Eckstein and Wiggers[11] found third sound vibrations in only 4 per cent if examined in the sitting posture, and in 26 per cent in the recumbent Auricular vibrations were found in 22 per cent in the sitting and 27 per cent in the recumbent.

The sound vibrations in each sound group vary with different individuals, both in health and disease. There is also considerable variation in any group of vibrations in successive beats Examples of normal heart sounds are shown in Figures 50, 51, 52, and 53

The *auricular component*, if present, consists of one to three vibrations which precede and merge immediately with the first ventricular sound. Its duration is about 0 04 to 0.06 second It is illustrated in Figure 50

The *first ventricular sound* is usually represented by the longest group of vibrations, varying between 5 and 11 Its duration is about 0.06 to 0.16 second Orias and Braun-Menendez[5] divided this group into four components. The first consists of one or two thick short vibrations immediately following the auricular sound The second is of higher frequency

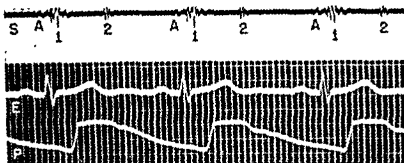


FIG 50.—SIMULTANEOUS RECORDINGS OF THE HEART SOUNDS, S, ELECTROCARDIOGRAM, E, AND BRACHIAL PULSE, P *Normal male* Spacing between any two parallel lines, 0 04 second Auricular component, A, lasting 0 06 second, precedes first sound Duration of first sound, 0.16 second, second sound, 0 06 second

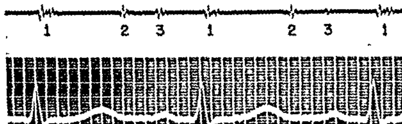


FIG 51—SIMULTANEOUS RECORDING OF THE HEART SOUNDS AND ELECTROCARDIOGRAM. Normal male presenting three heart sounds Duration of sounds first, 0 08, second, 0 05, and third, 0 05 second.

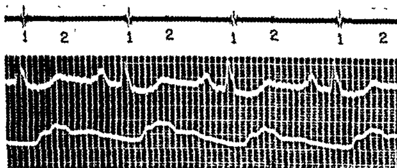


FIG 52—SIMULTANEOUS RECORDINGS OF HEART SOUNDS, ELECTROCARDIOGRAM AND BRACHIAL PULSE *Case of arteriosclerotic heart disease* Slight variations in the components of the first heart sound from time to time Second sound is of relatively low amplitude

The sound vibrations are transmitted to a resonator, the movements of which are recorded In the case of auscultation, the resonator is the tympanum of the ear and the recording is done by our auditory perception. In phonocardiography, the resonator is an artificial membrane, the movements of which are recorded either directly, by means of a suitable apparatus, or indirectly by transforming such movements into electric currents.

The indirect method is the one employed in present day phonocardiography. The sounds are transmitted to a microphone disc, the delicate diaphragm of which acts as a resonator which produce alternations in the current of an electric circuit These are recordable either by a string galvanometer or by a less sensitive oscillograph In the latter case, the electrical vibrations are first amplified by vacuum tubes.

Complete historical reviews of the development of the study of heart sounds by various authors may be found in the monograph by Orias and Braun-Menendez[5] and in the paper by Bierring, Bone and Lockhart[10] The description and the mode of operation of any given apparatus may be obtained from the manufacturer.

In registering the heart sound it is essential to eliminate all extrinsic sounds and noises in the room, and those caused by friction of the microphone on the chest caused by respiratory movements and by rubbing the microphone by an assistant's fingers

Phonocardiographic Tracings. In all tracings, two distinct groups of vibrations are observed representing the first and second sounds. In some cases, a third group is noted soon after the second group, representing the third heart sound and one or two short vibrations occur immediately before the first group, representing auricular contractions. In a study of 151 normal males, Boyer, Eckstein and Wiggers[11] found third sound vibrations in only 4 per cent if examined in the sitting posture, and in 26 per cent in the recumbent Auricular vibrations were found in 22 per cent in the sitting and 27 per cent in the recumbent.

The sound vibrations in each sound group vary with different individuals, both in health and disease. There is also considerable variation in any group of vibrations in successive beats. Examples of normal heart sounds are shown in Figures 50, 51, 52, and 53

The *auricular component*, if present, consists of one to three vibrations which precede and merge immediately with the first ventricular sound Its duration is about 0 04 to 0 06 second. It is illustrated in Figure 50.

The *first ventricular sound* is usually represented by the longest group of vibrations, varying between 5 and 11. Its duration is about 0 06 to 0.16 second. Orias and Braun-Menendez[5] divided this group into four components. The first consists of one or two thick short vibrations immediately following the auricular sound The second is of higher frequency

The *first and second ventricular vibrations* may show splitting of their respective groups in conditions described under auscultation. In the graphic records, however, the splitting is usually more easily visualized than is perceived by auscultation. In pulsus alternans, the frequency and amplitude of vibrations of the first and second sounds may increase and decrease in alternate beats.

The *third ventricular heart sound* shows the greatest amplitude and duration of vibrations in those cases where the sound is loud on auscultation. The greatest amplitude and duration occurs in protodiastolic gallop rhythm. Here it may be shown as a distinct group of sound vibrations separated from the second heart sound.

The Electrical Stethoscope

Within recent years, various devices have been developed for electrical amplification of the heart sounds. The amplified multiple stethoscope is being used for class instruction of several students who may listen to the heart simultaneously. Heart records may be recorded on gramophone discs and may be transmitted a long distance by telephone and radio. Although the heart sounds and murmurs thus amplified are more distinct than those heard in ordinary auscultation, their quality is not as good.

REFERENCES

[1] Rappaport, M. B., and Sprague, H. B.: Physiologic and physical laws that govern auscultation and their clinical application. Am. Heart J. 21: 257, 1941.

[2] Lewis, J. K., and Dock, W.: The origin of heart sounds and their variations in myocardial disease. J. A. M. A. 11: 271, 1948.

[3] Wiggers, C.: Physiology in Health and Disease. Philadelphia, Lea & Febiger, 1934.

[4] Wolferth, C. C., and Margolies, A.: Heart Sounds. Diagnosis and treatment of cardiovascular disease. W. D. Stroud, Editor, Chapter XXVI, Vol. 1. Philadelphia, F. A. Davis Co., 1940.

[5] Orias, O., and Braun-Menendez, E.: The Heart Sounds in Normal and Pathological Conditions. London, New York and Toronto, Oxford University Press, 1939.

[6] Wolferth, C. C., and Margolies, A.: Asynchronism in contraction of the ventricles in the so-called common type of bundle branch block: Its bearing on the determination of the side of the significant lesion and on the mechanism of split first and second heart sounds. Am. Heart J. 10: 425, 1935.

[7] Lewis, J. S.: The recruit's heart—Reduplication of the first sound. Heart strain and a new method of calibration. Am. Heart J. 30: 447, 1945.

[8] Lian, C., Marchal, M., and Pautrat, J.: Un signe clinique de la calcification du pericarde la vibrance pericardique protodiastolique. Bull. et mém. Soc. méd. d. hôp. de Paris, 49: 20, 1933.

[9] Hamman, L.: Spontaneous interstitial emphysema of the lungs. Tr. A. Am. Physicians 52: 311, 1937.

[10] Bierring, W. L., Bone, H. C., and Lockhart, M. L.: Use of the electrostethograph for recording heart sounds. J. A. M. A. 104: 628, 1935.

[11] Boyer, N. H., Eckstein, R. W., and Wiggers, C. J.: The characteristics of normal heart sounds recorded by direct methods. Am. Heart J. 19: 257, 1940.

CHAPTER IX

Cardiovascular Murmurs: Mechanism and Classification

MURMURS heard over the heart and blood vessels may, in some cases, be normal physiologic phenomena, not indicating organic cardiovascular disease In many others, however, where the murmur is pronounced, it indicates some structural abnormality To apply proper clinical significance to a given murmur, it is essential to understand its mode of production and its manifestations

Mechanism of Murmur Production

A murmur may normally be produced by an increase in the velocity of blood flow, or by a change in the viscosity of the blood In local pathologic conditions, it may result from a change in the direction of the blood flow, from impediments placed in its way and from a sudden constriction or dilatation of the tube through which the blood flows

Increase in the velocity of blood flow as a cause of murmurs is based on a simple fact of hydrodynamics When any fluid travels through a straight tube, the central portion, or axial stream, travels faster than the peripheral portion because of some degree of friction and cohesion of the latter at the vessel wall If the velocity of flow is not great, the difference in the speeds between the axial and the peripheral streams is not sufficient to produce disturbances If, on the other hand, the velocity is accelerated above a critical level, the difference becomes so marked as to set up eddies, Figure 54. These are perceived as murmurs The critical level at which this occurs, according to Bondi,[1] is a velocity of flow of over 200 centimeters per second.

Decreased viscosity of fluids, predisposes to the production of turbulence in its flow, which may be prerceived as murmurs Garb[2] has demonstrated the occurrence of murmurs when blood of low hemoglobin level is made to pass through an artificial tube Increasing its viscosity decreased the production of the murmurs

Changes in the direction of blood flow, caused by any impediment or abnormal opening will result in turbulence or eddy formation and thus in the production of a murmur. According to Bondi, "collision murmurs" develop in such cases as a result of vibrations produced when the current of blood impinges more or less perpendicularly upon a membrane-like tissue capable of vibration. The murmur of mitral insufficiency is perhaps partly due to such "collision" The blood current is directed through the defective

mitral valve back to the left auricle, striking the walls of the latter and giving rise to vibrations. Likewise, in mitral stenosis, the abnormal direction of the current towards the lateral wall of the left ventricle caused by the stenotic valve might partly be responsible for the murmur.

Murmurs from *impediments* to the free flow of blood by abnormal membranes or strings placed in its way may perhaps account for some of the heart murmurs caused by abnormalities in the chordae tendineae, as well



FIG 54 —FORMATION OF EDDIES DUE TO GREATER SPEED OF FLOW OF THE AXIAL THAN THE PERIPHERAL STREAM



FIG. 55 —MECHANISM OF COLLISION MURMUR Blood stream striking impediment is deflected against side of the wall of the vessel or heart



FIG 56 —MECHANISM OF MURMUR DUE TO SUDDEN CONSTRICTION OF THE VESSEL THROUGH WHICH BLOOD FLOWS There is an increase in the velocity of flow in the constricted area



FIG 57 —MECHANISM DUE TO DILATED PORTION OF VESSEL There is slowing of velocity of flow

as projections on the valves such as verrucae, The mechanism of murmurs produced by change in the direction of current flow and collision is shown in Figure 55.

Constriction or dilatation of any portion of a tube, through which fluids flow, will result in a sudden change in the velocity of flow and in the formation of eddies, as shown in Figures 56 and 57. Both these conditions will result in murmurs Impediments and constrictions are the main causes of murmurs in stenotic lesions of valves.

Methods of Determining Murmurs

Murmurs may be determined by auscultation and phonocardiography The auscultatory method is by far the more practicable and more efficient Phonocardiography cannot take its place for various reasons Although it may show the position of the given murmur in the cardiac cycle, it does not tell us in which valve it originates unless we place it over the valve areas where the murmur occurs, which in itself, must be determined by auscultation The transmission of the murmur, likewise, cannot be determined by the graphic method unless we follow the course of the murmur by repeated recordings obtained over different regions of the precordium Such a procedure is both impractical and inaccurate Furthermore, defects in two or more valve areas which may produce a variety of murmurs cannot be clearly analyzed in the phonocardiogram Phonocardiograms may, however, be of some value occasionally in following the progressive development of the disease of a given valve For this reason, some tracings are presented in this chapter illustrating systolic and diastolic murmurs.

In studying a murmur by auscultation, we must determine the time in the cardiac cycle in which it occurs, its location, area of transmission, its pitch, intensity and quality A murmur may often vary with the standing, sitting and recumbent postures of the patient In fact, in some cases, a given murmur may be heard when the patient is in one posture and not in another It may also vary with changes in respiration. These will be fully discussed under the various types of murmurs in this and later chapters

Classification of Murmurs

Murmurs heard over the heart are classified, according to the time in the cardiac cycle in which they appear, into systolic and diastolic. Murmurs produced in vessels close to the heart and transmitted to the heart region may also be systolic or diastolic in time relationship Often, however, they may be continuous, as in some cases of patent ductus arteriosus, arteriovenous aneurysm or venous hum

To assign significance to given murmurs due to valvular disease, they are classified according to their location into mitral, tricuspid, aortic and pulmonic The mitral murmurs are heard in their maximum intensity at the apex, the tricuspid at the xyphoid region, the aortic at the second right intercostal space close to the sternum, and the pulmonic at the second left intercostal space close to the sternum These regions are not the actual anatomic locations of the given valves but are areas on the surface of the chest where the structures transmitting the murmurs are closest to the chest wall. Figure 58 illustrates areas of the maximum intensity of murmurs on the surface of the chest in relation to the actual location of the valve orifices

Systolic Murmurs

Systolic murmurs are far more common than diastolic. They may be very short and fleeting, occupying only a short space in systole, or long,

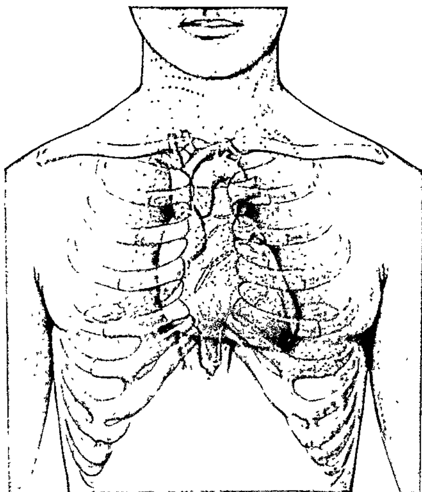


FIG 58—USUAL LOCATIONS AND TRANSMISSION OF MURMURS AND THEIR RELATION TO THE VALVE ORIFICES The intensity of each murmur in the given precordial area is represented by the density of the dots For description, see text

occupying the entire systolic period In the first case, they usually immediately follow the first sound and end long before the second sound, Figure 59 In the second case, they start at about the beginning of the first sound and

may extend to the very beginning of the second sound, Figure 60 In occasional cases, they may completely displace the first sound This is particularly true in a marked degree of calcific aortic stenosis when the entire systolic period may be occupied by a harsh, grinding systolic murmur, more marked at the base, and particularly at the aortic area

A systolic murmur may be blowing, rough, musical or grinding and of such low intensity as to be hardly audible or so loud as to be annoying to

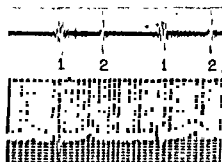


Fig 59—Apical Systolic Murmur, Short.

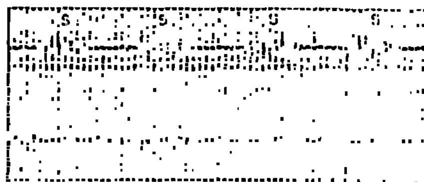


Fig 60—Long Systolic Murmur, S, Occupying the Entire Systolic Period From a female child, 6 years old, with congenital pulmonic stenosis

to the ear The intensity of the murmur, like its duration, depends upon the underlying pathologic process. A short and low intensity systolic murmur usually has no underlying structural disease. To this, there are exceptions. It may occasionally indicate more severe underlying heart disease, especially when it was previously loud. In such cases, it may indicate that the degree of the defect that produces the murmur has greatly increased or that myocardial failure has developed In some cases, where the valvular insufficiency is of extreme degree, the mechanism for murmur production may be lacking This occurs especially in severe congenital

heart disease with free communications between the right and left heart chambers, in which no murmurs may be heard.

Systolic murmurs may occur in the absence or presence of organic cardiovascular disease. The former are often spoken of as non-organic and the latter as organic.

Non-Organic Systolic Murmurs: These are probably the most frequently encountered, especially in childhood. They are usually very short, of low intensity and of varying quality. They have a tendency to change in their intensity from time to time, especially with changes in respiration and with posture. They are usually best heard in the dorsal or left lateral recumbent posture and at the end of expiration. They are not strictly localized to any so-called valve area, but they are often heard best over the pulmonic area. Occasionally, they are heard best at the apex, left sternal border or at the aortic area.

The causes of these murmurs undoubtedly vary in different cases, and under certain conditions. In childhood, thyrotoxicosis, febrile states, after exercise and excitement, where the heart rate is accelerated, an increased velocity of the blood flow is very likely the underlying cause of the murmur. When a murmur is heard in severe anemia, it is likely that a decrease in the viscocity of the blood as well as an increase in the velocity of the blood flow are the underlying causes. Where no such factors are present, and when the murmur is absent in the upright posture, but appears in the recumbent, the underlying cause may be interference with the normal course of the blood flow due to displacement of the pulmonic artery, aorta and heart chambers In slim and flat-chested persons where the murmur appears mainly at the end of expiration, it may be due to compression of the pulmonary artery by the anterior thoracic wall, constricting its lumen.

The *organic systolic murmurs* may be caused by actual structural mitral or tricuspid insufficiency or to relative insufficiency of these valves due to dilatation of the auriculo-ventricular rings. They may also be caused by aortic or pulmonic valve stenosis or by dilatation of the aorta or pulmonary artery in the regions above the valves. Congenital defects are occasional causes. All these will be fully discussed in Chapters XXIV and XXVII.

Diastolic Murmurs

In the great majority of cases, these are caused by organic valvular disease—auriculo-ventricular valve stenosis and aortic or pulmonic valve insufficiency. They occupy a variable time interval in the diastolic period and their characters and intensities vary with the extent of pathology of the given valves responsible for the murmur. In comparatively rare cases

they may be due to some dilatation of the aortic or pulmonic orifice caused by dilatation of the corresponding vessels They may at times also appar-

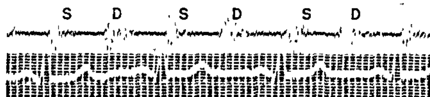


FIG 61 —FROM A MALE, 52 YEARS OLD, WITH LUETIC AORTIC INSUFFICIENCY AND ANEURYSM OF THE ASCENDING THORACIC AORTA Long diastolic murmur (D) due to aortic insufficiency and short systolic murmur (S) due to aortic dilatation.

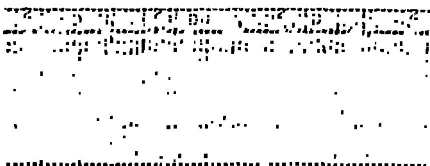


FIG 62 —DIASTOLIC MURMUR (D) OF MITRAL STENOSIS, OCCUPYING THE ENTIRE DIASTOLIC PERIOD WITH SLIGHT PRESYSTOLIC ACCENTUATION First heart sound (1); second heart sound (2) From a female, 33 years old, with old advanced mitral stenosis

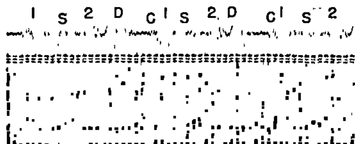


FIG 63 —FROM A FEMALE, 28 YEARS OLD, WITH MITRAL STENOSIS AND INSUFFICIENCY. Long systolic murmur, S, and high amplitude diastolic diminuendo murmur, D, with short crescendo phase, C, merging with the first sound of the next cycle 1, first sound, 2, second sound.

ently be caused by left or right ventricular dilatation without proportional dilatation of the corresponding auriculo-ventricular rings, thus producing the effect of relative narrowing. They are fully described in the chapter

on valvular disease. Examples of diastolic murmurs are shown in Figures 61 and 62.

Association of Systolic and Diastolic Murmurs: In many cases of multivalvular disease, systolic and diastolic murmurs occur over the given valve areas In the vast majority of cases, only the valves of the left heart are involved. Careful auscultation, coupled with palpation of a carotid artery for timing purposes, will in the majority of cases tell us which valve is involved and what form of involvement there is, whether pure stenosis or pure insufficiency or both. An example of murmurs occurring during systole and diastole is shown in Figure 63. In timing a murmur with the carotid artery pulsation anything we hear during the rise of the pulse in the carotid artery is systolic in time and anything we hear between the fall of the pulse and just before the next pulse rise is diastolic in time

Continuous Murmurs

Under this heading may be placed rare forms of murmurs transmitted to the heart region from disease in adjacent vessels. They have no definite time relationship to systole or diastole but consist of continuous noises throughout the cardiac cycle.

One of the conditions that often gives rise to such murmurs is patent ductus arteriosus, described in Chapter XXVII. It is usually spoken of as a "humming top," "mill wheel" or "machinery" murmur It may be associated with a thrill Some cases of patent ductus have only a systolic murmur.

Another condition that may be associated with a continuous murmur transmitted to the heart is an arteriovenous aneurysm in the vessels of the neck, or at the base of the heart or in the lungs

A third is the venous hum in the neck which has no pathologic significance The mechanism of this abnormal noise is not clearly understood. It may be due to rapid blood flow through the jugular veins into the superior vena cava It is heard loudest at the right base of the neck and is accentuated by turning or bending the head.

Pericardial Friction Rub

A pericardial friction rub is due to pericarditis caused by various conditions as discussed in Chapter XXV It may, in some cases, resemble an intracardiac murmur, especially when it is heard only during systole, as occasionally happens In most cases, it is heard during both systole and diastole, occupying a variable period during each phase It is differentiated from an intracardiac murmur by the following characteristics: It usually appears closer to the ear and is in most cases of a definite rubbing or grating quality. It may be extremely fleeting, appearing and disappearing in

the course of the examination or on different examinations on the same day and it is not localized to any definite valve area. It may be heard over various parts of the precordium and even in the back but it is most frequently heard close to the left sternal region and as far as the apex. At one time it may be very loud and rasping, assuming the quality of a leathery rub and a short time later it may be hardly audible. Occasionally, the rub may be felt by palpation

Pleuropericardial Murmurs

These may occasionally be mistaken for intracardiac murmurs They are caused by compression or by suction effect of the heart contraction on the adjacent portion of the lung. They may be recognized by their appearance and disappearance during various phases of respiration

REFERENCES

[1] Bondi, S. Die Entstehung der Herzgerausche. Ergebn inn. Med. Kinderheilk. 50 308, 1936.
[2] Garb, S.: The relationship of blood viscosity to the intensity of heart murmurs. Am Heart J 28:568, 1944.
[3] Flint, A. On cardiac murmurs. Am J M. Sc. 44:29, 1862.

CHAPTER X

Arterial and Venous Pulse: Normal and Abnormal

THE GRAPHIC recording of the arterial and venous pulse has been largely abandoned in clinical medicine This is due to the fact that some of the information obtained from the pulse record, such as the various cardiac arrhythmias, can be more easily gotten from the electrocardiogram. Also the possibility of technical errors is far less in the latter method Nevertheless, the pulse offers considerable information on the hemodynamics of the circulation in health and disease.

THE ARTERIAL PULSE

As discussed in Chapter IV, the arterial pulse is caused by the expulsion from the left ventricle of a volume of blood during systolic contraction. This volume is added to an already partly filled arterial tree and produces an expansion wave which travels through the arterial system, as shown before. Because of the constant diminution in the caliber of the arteries from the aorta down to the arterioles, their continuous branching and some differences in their distensibility, the shape of the pulse varies somewhat in different vessels However, if proper care is used in recording the pulse, it will be found to show considerable resemblance over various vascular regions in the same person

Recording the Pulse

The old method of recording the pulse consisted of applying a small receiver to the artery which picked up the pulsations and transmitted them by a lever to a revolving drum. More recent recording apparatus utilizes an air filled tambour which is placed over the artery Pulsation of the artery produces variations in the air pressure of the tambour. These pressure changes are transmitted by a rubber tube and are recorded on photographic paper. For the technic of pulse recording, the reader is referred to modern standard textbooks of physiology and to instructions given by the manufacturer who supplies the apparatus

and subcutaneous tissue overlying the artery, calcification, if present, and the sensitivity of the apparatus are factors which determine the appearance and accuracy of the tracing

The usual artery selected for study is the brachial or radial. The subclavian artery, if palpable, may be used with better advantages.

Factors Influencing the Arterial Pulse

Besides technical errors that may influence the appearance of the pulse, its height and configuration are influenced by inherent causes such as the force of ventricular contraction, the volume of blood ejected during systole, the distensibility of the arterial wall and the arteriolar resistance offered to the flow by the arterioles

Increased force of ventricular contraction, all other factors being equal, will eject the same volume of blood faster and will result in a higher pulse but one of shorter duration. Decreased force of ventricular contraction will result in an opposite effect

Increase in the volume of blood entering the left ventricle due to greater venous return, which occurs normally during exercise or on deep inspiration will result in greater left ventricular output and larger pulse. Diminished volume output due to decreased venous return, occurring normally during deep expiration and abnormally in shock or hemorrhage, will result in a weak or even imperceptible pulse.

All factors being equal, the pulse is higher in youth where the vessels are easily distensible than in older age groups where the vessels may be spastic or sclerotic

Increased peripheral resistance due to arteriolar spasm will result in a higher and more prolonged pulse Diminished peripheral resistance will result in a labile, short sustaining pulse.

Modification of the Pulse in Local Vascular Areas

There are instances also where the pulse may diminish in size or disappear over given vessels due to local conditions in the vessel or other factors. These must be borne in mind in applying significance to abnormalities of a given pulse and must not be mistaken for general circulatory disease. One of these factors is a congenital absence or aplasia of a given vessel. In the radial artery, this condition is very rare. In the dorsalis pedis and posterior tibial arteries, however, it occurs more frequently. Silverman[1] observed the absence of either the dorsalis pedis or the posterior tibial in 13 per cent of 1,014 normal healthy young infantry soldiers. The absence of the pulse in both arteries, however, occurred only in five cases. Another factor is a congenital displacement of an artery from its usual location. We must always search for the given artery in the immediate neighborhood before we consider it absent. Superimposition of fatty subcutaneous tissue over the given artery, as said before, may offer difficulty in palpating the pulse and give us a wrong impression of abnormality.

Important factors that may interfere with the normal pulse in the radial

or brachial arteries are the presence of local pathology in the thorax, such as an aneurysm, a mediastinal growth, localized atheroma or embolization. Conditions of this kind usually result in unilateral absence or diminished amplitude of the pulse It is essential, therefore, to examine the pulses in both arms simultaneously.

In aneurysm of the aorta, located at the origin of the innominate artery, the right pulse will be smaller than the left. If located at the origin of the left subclavian, the left pulse will be smaller and more delayed than the right

In mediastinal growth, the pulse will be affected on the side where the growth compresses the main artery in the thorax.

Diminished pulsation of the brachial and radial arteries on both sides may occur in the presence of accessory cervical ribs. These cases also often present signs of irritation of the brachial plexus such as pain and paresthesias.

In the great majority of normal individuals, the radial and brachial pulse will greatly diminish in size or entirely disappear by hyperabduction of the arms to an angle of 180 degrees. In some cases, marked backward fixation of the shoulders without abduction may produce the same results. The condition is caused by obliteration of the subclavian artery and compression of the brachial plexus, at the angle formed by the attachment of the scalinus anticus muscle to the first rib or by compression of these neurovascular structures at the point where they pass under the coracoid process and posterior to the pectoralis minor muscle. The obliteration of the pulse may partly be due to arterial spasm induced by the compression of the brachial plexus, as suggested by Wright [2] and Paull[3]. Wright observed some instances of gangrene of the fingers and paresthesias resulting from prolonged hyperabduction of the arms while sleeping in the supine positions

The Normal Arterial Pulse

The rate and rhythm of the normal pulse is the same as of the heart in the same individual Its size and shape, as determined by palpation, varies with the conditions mentioned above and can be easily ascertained in the individual case

An arteriogram obtained from the brachial or any other superficial medium-sized artery, shows a sharp, forwardly inclined upstroke followed by a progressive drop, interrupted temporarily by the dicrotic notch, Figures 64 and 65 The dicrotic notch represents approximately the time of closure of the aortic valves Besides this notch, there often appear small secondary wavelets on the descending limb which are probably due to artefacts and impacts caused by arterial branchings The height to which the upstroke rises depends upon the pulse volume.

The Abnormal Arterial Pulse

Abnormalities in the arterial pulse may be in the form of disturbances in the rate, rhythm, amplitude and shape. Disturbances in the rate and rhythm correspond to similar disturbances of the heart, described in Chapter VII

Disturbances in the amplitude and shape of the pulse assume different forms. We shall present here some of the more common forms of abnor-



FIG 64—SIMULTANEOUS ELECTROCARDIOGRAM AND ARTERIOGRAM OF THE BRACHIAL ARTERY Ascending limb of pulse begins about 0.16 second from the peak of the R wave in the electrocardiogram A dicrotic notch occurs high on the descending limb.

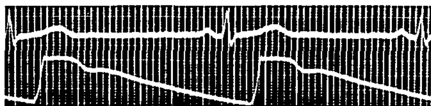


FIG 65—SIMULTANEOUS ELECTROCARDIOGRAM AND ARTERIOGRAM OF THE BRACHIAL ARTERY Marked slowing of the heart induced by carotid sinus pressure Amplitude of the arteriogram is higher and its duration longer than in Fig 64

malities For a more complete description, the reader is referred to Wiggers' paper[5] on the hemodynamic disturbances in various disorders.

The Alternating Pulse or Pulsus Alternans. This is occasionally observed in severe myocardial disease, especially of the arteriosclerotic type. It is characterized by a recurrence of alternate large and small pulses at a perfectly regular rhythm. The heart sounds do not vary from beat to beat and the electrocardiogram may or may not show alternation in the height of the complexes. In fact, electrical alternans occasionally occurs without pulsus alternans and its mechanism is probably different. Inasmuch as pulsus alternans usually indicates the presence of grave cardiac disease, its detection is of important prognostic significance.

In many cases, the alternations may be detected by careful palpation of the radial pulse. In most cases, it may best be elicited by the blood pres-

sure readings. The blood pressure cuff is inflated to a point above the systolic pressure and is then gradually deflated to a level where the systolic sound first appears. We will call this point the first level. On further deflation beyond this point, another level will be reached beyond which the number of beats heard will be double that of the first level.

The degree of pulsus alternans varies with the degree of heart disease. The greater the difference in the heights between the strong and weak pulses, the higher the degree of pulsus alternans and the more severe the myocardial disease The lower grades are in most cases very hard to detect by palpation of the pulse or even by blood pressure determination unless we are very careful in our examination. A properly obtained arteriogram, however, will reveal the condition at once, even in milder grades.

The physiologic mechanism of pulsus alternans is not definitely known It is assumed to be caused by fatigue of a portion of the heart muscle due to disease. This portion, therefore, does not fully contract at every other beat. The volume of blood discharged during the weaker beats is therefore smaller.

It is important to differentiate pulsus alternans from other conditions which may produce alternating strong and weak pulses because of the grave significance of the former. One of these is pulsus bigeminus, described in Chapter VII, which can be recognized by the character of the heart sounds as well as by the pulse spacings In pulsus alternans, the spacing between the higher and lower pulse is very slightly longer than that between the lower and the next higher pulse In pulsus bigeminus, the reverse is true

Another condition that may resemble pulsus alternans is *hyperdicrotism*, where the dicrotic waves may appear like small beats It is due to an exaggeration of the normal dicrotic wave. The pulse rises and falls abruptly, followed by a secondary shorter rise and rapid fall due to the dicrotic wave. The condition is very rare. It may be observed in severe, prolonged infectious fevers such as typhoid It is caused by a poor sustaining force of the heart contraction resulting in early closure of the semilunar valves followed by the rebounding force of the arterial pressure.

The Corrigan Pulse· This is characterized by a rapid rise and rapid fall of the pulse limbs, Figure 66 The condition occurs in its characteristic form in aortic insufficiency, although in milder form, it may occur also in marked peripheral vasodilatation, observed in thyrotoxicosis and in some forms of neurocirculatory disturbances Locally, it may be produced by the immersion of the limb in hot water.

In its characteristic form, when palpated over any palpable artery, it shows an abrupt, high rise and rapid fall to a very low level, leaving a feeling of emptiness in the artery between each pulse beat Its occurrence in aortic insufficiency was first described by Corrigan.[4]

The sudden high rise is due to the expulsion by the left ventricle of a greater volume of blood during systole than in normal conditions. This greater volume results from the regurgitant blood coming from the aorta during diastole adding to the volume entering from the left auricle The sudden collapse of the pulse is due partly to the regurgitation and partly also to reflex peripheral vasodilatation. The latter is evidenced by the capillary pulsation observed in these cases.

As a result of rapid overfilling and rapid emptying of the arteries, the blood pressure is characterized by a high systolic and a very low diastolic level. The systolic level may reach, in some cases, as high as 200 millimeters of mercury or even higher and the diastolic level 50 millimeters or



Fig 66 —Modified Corrigan Pulse There is an abrupt rise of the ascending limb and comparatively rapid fall of the descending limb From a case of low grade aortic insufficiency

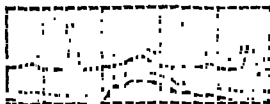


Fig 67 —Comparatively Slowly Rising and Long Sustaining Brachial Pulse from a Case of Low-Grade Aortic Stenosis

less, resulting in a very high pulse pressure In some cases, we may get a so-called zero diastolic reading although complete emptying of the arteries, of course, never occurs

The Slowly Rising and Long Sustaining Pulse· Often spoken of as the *pulsus parvus tardus and rarus*, this is almost pathognomonic of aortic stenosis. Figure 67 is a modified example, the pulse wave rises slowly, reaches a low level plateau which is of comparatively long duration, and then recedes slowly On palpation, the pulse is very small and of comparatively long duration. The systolic blood pressure is low and the diastolic may be within normal limits, resulting in a low pulse pressure.

The condition is caused by interference with the free entrance of blood from the left ventricle into the arterial tree during systole, due to the

stenosis. Reflex peripheral vasoconstriction also may perhaps play a part in maintaining a relatively normal diastolic level.

The Pulse in Shock. In severe cases of shock or hemorrhage, the pulse, as felt over the radial artery, is very small, thready and may become imperceptible from time to time If the condition is progressive, it will disappear entirely for a variable period before death.

The "Paradoxical Pulse": This pulse frequently occurs in extensive adhesive pericarditis or in massive pericardial effusion and may help in the diagnosis of these conditions. It is characterized by a diminution or the entire disappearance of the pulse with inspiraton and reappearance with expiration It is assumed to be caused by stretching and distortion of the vena cava during inspiration which together with the auricles are already greatly compressed by the effusion or adhesions The increased stretching or distortion further prevents auricular filling, resulting in a diminished ventricular output.

The term "paradoxical" is used to describe this pulse because under normal conditions, with predominant diaphragmatic respiration, the size of the pulse is increased during inspiration and decreased during expiration. It must be remembered, however, that even in normal individuals, purely costal breathing may decrease the amplitude of the pulse slightly during inspiration and increase during expiration

The Venous Pulse

The venous pulse can best be studied by obtaining a careful tracing or phlebogram. It is hard to analyze this pulse by inspection of the jugular veins

A properly obtained phlebogram expresses the pressure changes in the right auricle and is therefore of value in understanding the mechanism of cardiac action With the advent of electrocardiography, phlebography has been almost entirely abandoned by the clinician, for much of the information that we can obtain from the phlebogram can more easily be obtained from the electrocardiogram. Nevertheless, the phlebogram has its place in the study of the dynamics of the circulation and even in elucidating some abnormalities in the electrocardiogram.

Obtaining of Phlebogram

The best location to obtain a jugular pulse tracing is over the right jugular bulb lying just above the inner end of the right clavicle. A disclike receiver is applied to the skin in that region, the lower end resting on the clavicle, making sure that the skin makes an air-tight contact with the disc. The disc is connected with a rubber tubing which leads to the recording

apparatus. Changes in the pressure of the jugular bulb produce changes in the air pressure in the apparatus which is recorded

In recent years, ingenious methods of direct recording of the shadow of the pulsating jugular vein or the recording of the movements of a beam of light from a minute mirror attached to the skin over the vein have been devised. The reader is referred to modern textbooks on physiology for details.

In every method employed, it is important to have the person in a position that will assure some fullness of the jugular bulb. In normal individuals, this can best be accomplished with the subject in the dorsal recumbent position and head retracted slightly backwards. In cases of congestive failure, however, where the veins in the neck are overdistended, it is best

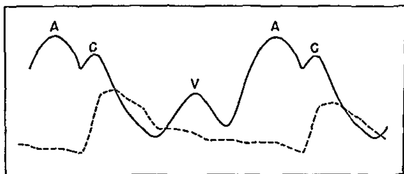


Fig 68—A Normal Phlebogram (Solid Line) in its Time Relationship to a Normal Arteriogram (Broken Line)

to have the patient in a semirecumbent posture. Each case must be tested carefully for the best position

The Normal Phlebogram

This consists of three main waves: the "A," "C" and "V" waves, respectively, Figure 68

The "A" wave is due to auricular systole. Its size varies with the force of auricular contraction, with the position of the subject and with the volume of blood in the vein. It is characterized by a rise to a variable level followed by a sloping drop due to auricular diastole which empties the adjacent veins

The "C" wave follows the "A" wave by an interval of about 0 14 to .20 second and corresponds to the period of ventricular systole. It is caused partly by the ventricular contraction which transmits a wave impluse up to the right auricle, the vena cava and the jugular vein The main cause is the transmission of the carotid pulse to the adjacent jugular vein. The size of the "C" wave depends upon the force of ventricular contraction,

the expansile distention of the carotid artery, the position of the patient and the manner of application of the disc to the jugular bulb Light external pressure applied to the disc will register mainly the venous pressure changes Stronger external pressure will obliterate the jugular bulb and will register only the arterial pulsation.

The "V" wave is due mainly to stasis in the right auricle caused by the gradual accumulation of blood in that chamber during ventricular systole. The accumulated blood in the right auricle reaches its maximum at the end of ventricular systole, just before the opening of the auriculo-ventricular valve. This wave ends with the opening of the auriculo-ventricular valves and the emptying of the auricular and adjacent venous blood into the ventricles, producing the sloping descending limb of the "V" wave.

The Abnormal Phlebogram

As said before, the use of the phlebogram in the study of the various arrhythmias has been all but abandoned because of the greater ease and less possible sources of error in electrocardiography employed for that purpose. It may, however, occasionally elucidate certain conditions which the electrocardiogram leaves in doubt.

Eliminating technical errors and positional factors which may modify the "A" wave, an accentuation in the height of this wave may signify an increase in the blood volume or an increase in the amplitude of auricular contraction A diminution in the size of the "A" wave would speak for diminution in the power of auricular contraction such as may occur in marked auricular stasis. The absence of an "A" wave would speak either for auricular paralysis, if the ventricular rate is regular or for auricular fibrillation if irregular. Where the "A" wave falls regularly on the "C" or "V" wave, accentuating the latter, it would point to nodal rhythm and would thus help in this diagnosis if the P wave is not visible in the electrocardiogram

A marked exaggeration of the "C" wave may indicate the presence of either tricuspid insufficiency or an arteriovenous aneurysm between the aorta and superior vena cava Both are extremely rare conditions and can be recognized by other signs, to be discussed in later chapters.

The "V" wave will be more prominent than normal in venous stasis If the stasis becomes extreme, the "V" wave will merge with the "C" wave, forming a broad somewhat irregular plateau.

Occasionally, other small waves are observed, the origin of which is not fully understood.

It will thus be seen that the usefulness of phlebography in clinical diagnosis is limited Most of the conditions in which it is of help in diagnosis can be recognized by physical findings

REFERENCES

[1] Silverman, J J The incidence of palpable dorsalis pedis and posterior tibial pulsations in soldiers An analysis of over 1,000 infantry soldiers. Am Heart J 32 82, 1946
[2] Wright, I. S. The neuromuscular syndrome produced by hyperabduction of the arms. Am Heart J 29 1, 1945
[3] Paull, R The neuromuscular syndrome as manifested in the upper extremities Am Heart J 32 32, 1946
[4] Corrigan, D J On permanent patency of the mouth of the aorta, or inadequacy of the aortic valves Edinburgh M. & Surg J 37 225, 1832
[5] Wiggers, C J Basic hemodynamic principles essential to interpretation of cardiovascular disorders Bull New York Acad. Med 18 3, 1942

CHAPTER XI

Normal Arterial and Venous Blood Pressure

THE INTRODUCTION within the past 50 years of indirect methods of determination of arterial and venous blood pressure has done much in elucidating the dynamics of the circulation in health and disease.

The measurement of blood pressure in the human can be accomplished only over peripheral palpable vessels For this reason, only the systemic blood pressure can thus be determined The pulmonic arterial or venous blood pressure cannot be investigated directly. In presenting the available facts of the arterial and venous blood pressure in this chapter, we refer, therefore, only to the systemic blood pressure.

Although there is some variation in the blood pressure in the various peripheral vessels, readings obtained over a large-sized vessel give us a good idea of the average systemic pressure

ARTERIAL BLOOD PRESSURE

The arterial blood pressure is measured by the sphygmomanometer, of which there are two kinds—the mercury and the spring. In the mercury sphygmomanometer, the blood pressure is determined by the rise of a column of mercury to a given height in millimeters In the spring apparatus, the pressure is registered by a needle on a carefully calibrated dial. These are the ordinary apparatus universally employed in practice.

There are also various sphygmomanometers obtainable for special uses, built on the principle of the spring apparatus. Of these, there is the recording apparatus, which produces a permanent record of the blood pressure variations, and the oscillometer for registering the pulse fluctuations at various blood pressure levels. The latter is used in the study of peripheral vascular disease

The Determination of the Arterial Blood Pressure

The usual location for obtaining the arterial blood pressure is over the brachial artery. An armlet which encloses a rubber bag is placed firmly around the arm above the bend of the elbow. The rubber bag has two rubber tubes leading from it—one to a pump or rubber bulb and the other to the mercury or spring manometer, whichever is used. The rubber bag is inflated by the pump to the point of obliteration of the radial pulse. The bag is then gradually deflated while we listen with a stethoscope at the antecubital space over the brachial artery for sounds. The millimeter mark at which the sounds first appear represents the systolic pressure.

These undergo certain variations in intensity and quality until they entirely disappear. The point of complete disappearance of the sound represents the diastolic pressure. Some observers consider the diastolic pressure at a point when the sound becomes greatly diminished in intensity, just before its complete disappearance

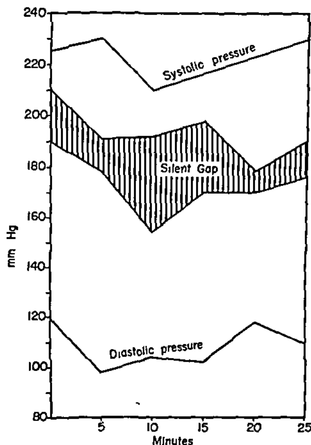


FIG 69—"SILENT GAP" IN BLOOD PRESSURE READINGS Six blood pressure determinations at five minute intervals in male, with hypertension presenting this "gap" Fluctuations are noted in the systolic and diastolic pressures and in the upper and lower levels of the "gap." See text

In the past, there has been a tendency to divide the various types of sounds heard between the systolic and diastolic levels into four phases. Such division is of no practical importance and may be disregarded We must bear in mind the fact, however, that in comparatively rare conditions, mentioned in a previous communication,[1] a portion of the blood pressure sounds in hypertension may disappear soon after the maximum systolic

pressure reading and reappear again after a gap of 5 to 40 millimeters. This is known as the "silent gap," shown in Figure 69. Its importance lies in the fact that if we do not inflate the bag above the actual systolic blood pressure, we may mistake the lower level of the gap for the systolic pressure.

Mechanics of Blood Pressure Registration and of the Sounds Produced

The registration of blood pressure, in terms of millimeters rise of mercury, is dependent upon the counterbalancing effect of the external pressure by the inflated bag upon the intra-arterial pressure. Inasmuch as the former is equivalent at any moment to the latter, the height of the rise of the column of mercury measures the intra-arterial pressure at that moment.

The production of the sounds or murmurs over the brachial artery is caused by the compression which slows the blood stream in the segment of the constricted artery. This results in the formation of eddies and in vibration of the vessel wall which are transmitted to the ear in the form of sound waves, as described in Chapter VII. The amount of compression determines the extent of slowing of the stream and the vibration of the vessel wall, therefore the types of sound heard.

Standardization of Blood Pressure Determinations

A proper registration of blood pressure requires careful technic. In order to adopt a uniform method, the American Heart Association and the Cardiac Society of Great Britain and Ireland[2] have adopted certain standards for determining the blood pressure In brief they are as follows:

The blood pressure apparatus should be calibrated at yearly intervals or oftener if defects are suspected. The patient must be comfortably seated, arm slightly flexed and forearm supported at the level of the heart on a smooth surface The arm above the armlet must have no constriction of clothes. Before the pressure is determined, the patient must rest a while. The cuff containing the rubber bag should be about 12 to 13 centimeters wide. For children under 8 years, the rubber bag should be 9 cm and under 4 years less than 6 cm. The bag should be completely deflated before it is applied to the arm It should be placed snugly over the inner aspect of the arm, the lower edge of the cuff extending to about one inch above the antecubital space. There should be no bulging or displacement of the rubber bag. Palpation should always be used as a check on the auscultatory readings and if the systolic pressure, as determined by palpation, is higher than the auscultatory reading the former reading should be accepted as the systolic pressure. The stethoscope is to be placed lightly on the brachial artery, not in contact with the cuff. We must be sure

that there is no opening between the stethoscope bell and the skin. The cuff should be rapidly inflated to a pressure of 30 mm. above the level at which the radial pulse can be palpated. Deflation should be in slow steps of 2 or 3 millimeters per second. The level at which the first sound regularly appears should be considered the *systolic pressure*, unless the palpatory level is higher. The point at which the sound suddenly becomes dull and muffled should be considered the *diastolic pressure*. On this point the American and British Committees disagree The former recommends the point of complete disappearance of the sound as the diastolic pressure. The determination is to be done in as short a time as possible to avoid prolonged compression of the arm and venous congestion. On the first examination, it is suggested that the blood pressure be taken on both arms. If there is marked variation in the readings with respiration the pressure should be determined rapidly while the patient holds his breath in mid-respiration.

In some cases such as in suspected coarctation of the aorta, it is important to determine also the arterial blood pressure in the leg For this purpose, the committee recommends that the rubber bag should be 15 cm. wide and its covering 17 cm. wide

Normal Arterial Blood Pressure

By normal arterial blood pressure we mean pressure levels observed in perfectly normal individuals with no demonstrable cardiovascular disease. Such blood pressure levels do not always indicate that the cardiovascular system is normal. In many cases of cardiovascular disease, the blood pressure may be within normal limits. On the other hand, slight to moderate hypertension may exist in some cases for many years with no apparent ill effects The importance of blood pressure findings is therefore not to be overestimated or overemphasized.

Range of Normal Arterial Blood Pressure: According to the numerous reported series of cases the systolic and diastolic pressure levels vary with age and sex. The most representative series of large numbers of cases for infancy and childhood are those reported by Rucker and Connell,[3] Judson and Michaelson,[4] and Faber and James[5] For university students the report by Alvarez and co-workers,[6] and for older adults, middle age and old age by Saller[7] are noteworthy

From the above and other reported series of cases as well as from personal observations, the following levels may be considered to be within the normal range at the various ages: At birth, the systolic blood pressure varies between 40 to 55 millimeters of mercury for both sexes. By the end of the first month it rises to about 60 to 75 millimeters. Thereafter, the rise is much more gradual. It reaches an average of about 90 milli-

meters by the ninth year and 100 to 115 millimeters by the fourteenth year. The diastolic pressure ranges between 60 and 75 mm. at this period. Between 16 and 18 years, the systolic blood pressure is about 130 mm. for men and about 118 mm. for women. There is then a tendency for it to drop in both sexes to a somewhat lower level up to 24 years of age and rise again up to 40 years and in later life. The higher blood pressure levels often observed between 16 and 18 years of age is probably due to greater sensitiveness of the sympathetic nervous system associated with greater fluctuations in emotions at this time in life

The average blood pressure between 25 to 40 years is between 120 and 140 systolic and 80 to 85 diastolic. Between 40 and 65, the maximum normal is about 150 systolic and 90 diastolic.

It is important to bear in mind the fact that the lower limit of normal systolic blood pressure for the adult and middle age groups is about 90 millimeters while the upper limit is 150. Although the former figure is comparatively infrequent its finding in an individual with no complaints should not alarm the examining physician.

Normal Variations in Blood Pressure: In any normal individual, there is a tendency for the blood pressure to fluctuate under various conditions. This tendency appears to be greater in some individuals than in others, depending upon the sensitivity of the sympathetic nervous system.

Among the factors that bring about an increase in the blood pressure, both systolic and diastolic but more so the former, are physical exertion, emotional upset and digestive processes. Tobacco smoke produces a temporary rise Change in posture from the recumbent to the standing positions may produce some rise in pressure Complete rest and sleep will lower the pressure.

One important fact to remember is that spontaneous fluctuations in the blood pressure may occasionally be observed even at perfect rest. The fluctuations in the systolic and diastolic levels are not equal at any given moment. Thus, the systolic level may rise while the diastolic will fall or remain stationary during any given blood pressure determination. At times, both rise or both fall at the same time, but not to the same extent As a result of the differences in the systolic and diastolic fluctuations, the pulse pressure shows some variation from time to time The greatest fluctuations occur in the presence of early essential hypertension. In normal individuals who at no time show an abnormal elevation in pressure, the fluctuations are trivial.

The author has followed a number of cases whose blood pressure levels were normal, but who showed an occasional slight spontaneous rise above the normal levels. In the course of five to eighteen years, nearly all developed a variable degree of hypertension. Although the number of cases

that there is no opening between the stethoscope bell and the skin. The cuff should be rapidly inflated to a pressure of 30 mm. above the level at which the radial pulse can be palpated Deflation should be in slow steps of 2 or 3 millimeters per second. The level at which the first sound regularly appears should be considered the *systolic pressure*, unless the palpatory level is higher. The point at which the sound suddenly becomes dull and muffled should be considered the *diastolic pressure*. On this point the American and British Committees disagree. The former recommends the point of complete disappearance of the sound as the diastolic pressure. The determination is to be done in as short a time as possible to avoid prolonged compression of the arm and venous congestion. On the first examination, it is suggested that the blood pressure be taken on both arms If there is marked variation in the readings with respiration the pressure should be determined rapidly while the patient holds his breath in mid-respiration

In some cases such as in suspected coarctation of the aorta, it is important to determine also the arterial blood pressure in the leg For this purpose, the committee recommends that the rubber bag should be 15 cm. wide and its covering 17 cm wide.

Normal Arterial Blood Pressure

By normal arterial blood pressure we mean pressure levels observed in perfectly normal individuals with no demonstrable cardiovascular disease. Such blood pressure levels do not always indicate that the cardiovascular system is normal In many cases of cardiovascular disease, the blood pressure may be within normal limits. On the other hand, slight to moderate hypertension may exist in some cases for many years with no apparent ill effects The importance of blood pressure findings is therefore not to be overestimated or overemphasized.

Range of Normal Arterial Blood Pressure· According to the numerous reported series of cases the systolic and diastolic pressure levels vary with age and sex. The most representative series of large numbers of cases for infancy and childhood are those reported by Rucker and Connell,[3] Judson and Michaelson,[4] and Faber and James.[5] For university students the report by Alvarez and co-workers,[6] and for older adults, middle age and old age by Saller[7] are noteworthy

From the above and other reported series of cases as well as from personal observations, the following levels may be considered to be within the normal range at the various ages: At birth, the systolic blood pressure varies between 40 to 55 millimeters of mercury for both sexes. By the end of the first month it rises to about 60 to 75 millimeters. Thereafter, the rise is much more gradual. It reaches an average of about 90 milli-

The Mechanism of Venous Pressure

The venous pressure is partly due to the residual of the original head of pressure imparted to the column of blood by the ventricular contraction and partly also to the hydrostatic pressure caused by gravity.

Because of the effect of gravity, the venous pressure is much greater in the lower than in the upper part of the body. If the lower limbs are perfectly relaxed, with the person in the upright posture, the effect of gravity is such that it may temporarily stop the flow of blood through some of the veins The valves come into play to prevent the backflow towards the capillary side under such circumstances and resumption of muscular activity again empties these veins towards the heart Gravity is an important cause of the pathogenesis of phlebothrombosis

There are two factors that keep the venous pressure in a stable form under normal conditions; namely, the variability in the amount of blood pumped by the heart and the changing capacity of the peripheral vascular bed As described in Chapter IV, increased somatic muscular activity produces arteriolar and capillary dilatation in the active muscles, resulting in a greater flow of blood towards the veins and thence towards the heart. The massaging effect of the muscles on the veins helps such venous flow. The heart, receiving more blood, responds to the physiologic stimulus of larger volume by greater contraction so that the cardiac output becomes greater. The net result is that the venous side of the circulation is kept stable.

Measurement of Venous Pressure

Because of the marked effect of gravity and muscular activity on the venous pressure, its measurements should be done in the recumbent or semirecumbent posture, at perfect rest The right arm, where the determination is usually done, is placed so that any prominent superficial vein in the forearm used should be on a level with the right auricle.

There are two methods employed, the direct and indirect. In the direct method, a needle connected by a rubber tube with a water manometer is inserted in the vein and the measurement is determined by the height to which the water rises, measured in millimeters. Recently, Winsor and Burch[11] introduced a spring manometer similar to that used for arterial blood pressure determination but graduated to the scale of a water manometer It has the advantage over the water manometer in not requiring the injection of fluid in the vein and in being able to record the venous pressure in small as well as in large veins.

The reason why a water rather than mercury scale is used in the direct method is that the venous pressure is so low that it is hard to record by a counterweight of mercury. Mercury is 13.5 times heavier than water.

The indirect method consists of compressing the vein enough to obliterate the blood flow completely and determine the amount of pressure required to do that. It is based on the principle that outside pressure applied to a superficial vein will stop the venous flow if it equals the pressure within the vein. An improved apparatus used for that purpose is that of Eyster, a full description of which is to be found in his monograph.[12]

Range of Venous Pressure

The values for the *normal* venous pressure are approximately the same for each method used. In the recumbent posture, as measured in the arm at rest, it is usually 40 to 60 millimeters of water but may in some cases be as much as 110 millimeters. In the sitting posture, it is usually about 75 to 80 millimeters but may reach 140 millimeters In the upright posture, it may be as high as 180. During exercise, it may reach 170 to 220 mm. Winsor and Burch[11] found the venous pressure to be higher in males than in females. They also found it to be higher in the morning It rises with expiration and falls with inspiration It is increased by the Valsalva experiment. In the ankle and in the dorsal pedal veins, it is higher than in the arm, being about 150 in the ankle and 178 in the dorsal pedal It is always increased when the needle is first inserted, due to venous spasm.

Venous pressure is considered *abnormal* and indicates cardiac failure when it is above 200 mm under basal conditions This is true if physiologic factors such as forced breathing are eliminated as a cause of the increased pressure A rising venous pressure above this level means that the heart is failing rapidly. A falling pressure indicates restoration of the cardiac reserve.

REFERENCES

[1] Sigler, L. H.. Spontaneous nonrhythmic variations in the blood pressure levels and in the "silent gap." A theory of vasomotor arrhythmia Am J. M Sc 177-494, 1929

[2] Standardization of blood pressure readings Am Heart J 18-95, 1939

[3] Rucker, M. P, and Connell, J W · Blood pressure in the new-born Am J Dis Child 27:6, 1924.

[4] Judson, C. F, and Nicholson, P.. Blood pressure in normal children Am J. Dis. Child 8:257, 1914.

[5] Faber, H. K., and James, C A.· The range and distribution of blood pressures in normal children. Clinical application of statistical methods to the interpretation of deviation from the normal average Am. J. Dis. Child 22-7, 1921

[6] Alvarez, W. C, Wulzen, R., and Mahoney, L. J : Blood pressures in fifteen thousand university freshmen Arch. Int. Med 32.17, 1923

[7] Saller, K.. Über die Altersveränderungen des Blutdrucks. Ztschr f d. ges. exper Med. 58-683, 1928.

[8] Hines, E. A, Jr, and Brown, G E.. The cold pressor test for measuring the reactibility of the blood pressure Data concerning 571 normal and hypertensive subjects Am. Heart J. 11:1, 1936

[9] Russek, H. I., and Zohman, B. L.: Influence of age upon blood pressure response to the cold pressor test. Am. Heart J. 29:113, 1945.
[10] Kay, W. E., and Gardner, K. D.: Comparative blood pressure in the two arms. California and West. Med. 33:578, 1930.
[11] Winsor, T., and Burch, G. E.: Use of the phlebomanometer: Normal venous pressure values and a study of certain clinical aspects of venous hypertension in man. Am. Heart J. 31:387, 1946.
[12] Eyster, J. A. E.: The Clinical Aspects of Venous Pressure. New York, The Macmillan Co., 1929.

CHAPTER XII

Subjective Manifestations of Heart Disease

We have discussed, so far, the various objective findings in the cardiovascular system in health and the modifications that may occur in disease. A thorough understanding of these findings is very important for a proper diagnosis of cardiovascular disease. Of greater importance, however, are the subjective manifestations of disease or the complaints of the patient. Here, we enter an intangible realm which often requires the ingenuity of the examiner to unravel properly The individual reaction to disease varies widely in different patients. Comparatively trivial deviations from the normal anatomic state or physiologic functions may result in a train of symptoms in the neuropath or psychopath that baffles the examiner. On the other hand, gross structural disease or marked physiologic disturbances may occur in other cases with practically no complaints by the patient

In evaluating the patient's complaints, it is important, therefore, to get first of all a clear mental impression of the individual The manner in which he recites his story, his detailed analysis of each complaint, the wide diversity of complaints, out of proportion to objective manifestations, his clamoring for attention and his description of symptoms not in conformity with those expected to occur in various forms of cardiovascular disease, will help determine the extent of the neurogenic element in the case Also, the kind of symptoms and the manner in which they are brought about, if uncolored, will give us a clue to the type and extent of cardiovascular disease from which the patient suffers.

Various forms of structural disease of the heart and great vessels may exist in some cases for many years without any subjective disturbances. The patient may first become aware of some disturbances only after being told by a misguided physician or by an insurance examiner that he has some organic heart disease or a murmur.

An excellent example is a female first observed when she was 68 years old. She complained at that time of pain in the upper sternal region, not related to exertion, dizziness, palpitation, lack of energy and nauseous feeling. Most of the symptoms developed after she was told by a physician that she had a murmur and had received digitalis and aminophylline. When first seen by the author 10 months later, she presented a low grade hypertension with atherosclerosis and some dilatation of the aorta. There was no evidence of gross structural myocardial disease or insufficiency. The electrocardiogram showed abnormalities characteristic of

digitalis intoxication. After reassurance and the discontinuance of medication, all symptoms subsided. At the present writing, four years later at the age of 72, she still enjoys normal health

It must be understood, however, that any form of organic cardiovascular disease may sooner or later produce symptoms. Even such cases, however, frequently develop a fear complex, as would naturally be expected, which aggravates the symptoms due to heart disease. Also, other bodily disease or disturbance may present symptoms simulating those of heart disease. For these reasons, it is at times difficult to determine how much of any given symptom or symptom-complex is due to heart disease and how much to other disturbances

The subjective manifestations of heart disease may be divided into primary and secondary.

The Primary Manifestations: These are caused by failure of the myocardium itself, failure of the coronary blood supply to the myocardium and *failure in the delivery of blood to the cerebral centers* Many manifestations may be caused also by peripheral circulatory failure, to be discussed in Chapter XVI, and by the tachycardias and arrhythmias discussed in Chapter VII.

The subjective manifestations due to *failure of the myocardium* consist of dyspnea, orthopnea, "cardiac asthma," cough, Cheyne-Stokes breathing, cyanosis and peripheral edema. The degree of such symptoms is in direct proportion to the degree of failure and the location where failure is most prominent It is understood that nearly all of these manifestations are also objective and the extent of cardiac failure can thus be determined in advanced cases by a proper physical examination.

Subjective manifestations caused by *failure of the coronary blood supply* consist of more or less characteristic precordial pain or a sense of constriction with characteristic radiation and a train of other sensory disturbances to be discussed in Chapter XIV. In most cases, the manifestations are entirely subjective, as there may be no objective findings to corroborate the patient's complaints. In severe cases, of course, if observed during an acute episode, there may be some signs substantiating the patient's suffering, such as a cold sweat, pallor, shock and other manifestations to be discussed later.

Failure of the blood supply to the cerebrum is characterized, among many other disturbances, by sensations of dizziness, a stuporous state, loss of power of concentration and orientation, coma and convulsions The degree of these manifestations is in direct proportion to the degree of cerebral ischemia

The Secondary Manifestations: These consist of numerous complaints which, in many cases, are not directly attributable to the pathologic state

of the heart. They may consist of general vague aches and pains, digestive disturbances, palpitation, marked nervousness, irritability, psychic disturbances and a great many other complaints Some of these may be due to indirect effects of the circulatory disturbances on various parts of the body resulting in interferences with the normal bodily functions. In many others, they may be traced to psychologic disturbances incident to disease and the fear of its consequences In most cases, they are probably caused by both of these factors and possibly many other conditions. For instance, focal infection, deprivation of various nutritious materials incident in some cases to restricted diet, overfeeding, and the excessive use of coffee and tobacco. These may all play their part in some cases

In the following three chapters, we shall discuss the primary manifestations of heart disease more fully The secondary manifestations will be discussed later, when the various diseased states will be described

CHAPTER XIII
Heart Failure

Before proceeding with the description of the manifestations of heart failure, we must have some understanding of its mechanism

Mechanism of Heart Failure

By heart failure, we mean the inability of the heart to expel the entire volume of blood entering its chambers This inability is due to failure of the myocardium to carry on its function of contraction in an efficient manner. The degree of failure is measured by the extent of impairment of such function.

The contraction of heart muscle, like that of somatic muscle, is accompanied by a release of energy which manifests itself in the production of heat and in mechanical work performed The amount of work performed may be expressed mathematically by the extent of its contraction, measured by its shortening, multiplied by the load it carries That is, work = weight of load × height to which it is lifted When so measured, it will be found that within normal physiologic limits, the greater the load the muscle has to lift, the more the muscle fibers stretch and the greater the force of the muscular contraction, as determined by the height to which the load is lifted The amount of mechanical work performed under various loads, however, is governed, within limits, more by the weight of the load than by the height to which it is lifted That is, the greater the load, the more the muscle is stretched, although the height to which the load is lifted may become less due to insufficient muscular rebound A point is soon reached when the weight of the load exceeds the limit of ability of the muscle to lift it when stretching of the muscle fibers will occur without performing any work

These are essentially the steps in the development of muscular failure and may be applicable to the heart muscle as well as to somatic muscle Prolonged gradual activity with periods of rest between, to prevent fatigue, will result in temporary stretching of the muscle followed by increased contraction This may eventually result in muscle fiber hypertrophy In other words, slight dilatation, expressed by stretching, is followed by hypertrophy. As the process progresses, the amount of work the same muscle can perform will be progressively greater This is what happens under proper training If an unusually heavy load is thrown abruptly on the muscle without previous adaptation, dilatation of the muscle will occur without performing any appreciable work This may also occur when

the load is not excessive but if the blood supply to the muscle is inadequate or the muscle is not in a healthy state.

In the case of the heart muscle, the stimulus to efficient contraction is the load of the returning venous blood to the heart. Increased bodily activity results in an increase in the venous return of blood to the heart from the contracting somatic muscles This increased volume puts the heart muscle fibers under greater tensile force, resulting in an increase in the amplitude of cardiac contraction and, therefore, greater expulsion of blood, as described in Chapter IV It also produces reflex acceleration of the heart, resulting in more frequent emptying.

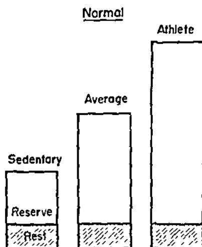


Fig 70—Rest Force and Reserve Force of the Normal Heart in Individuals with Various Occupational Pursuits Reserve force is greater in those who live an active life It may partly be explained by a desire of constitutionally inferior individuals to avoid excessive activity

For convenience of description, we speak of the force or power of ventricular contraction, with a person at rest, as the *rest force* and that under activity as the *reserve force* of the heart muscle. In normal individuals the reserve force varies to a great extent with the general health of the person, and with the type of life he has been living, whether sedentary or active. A person whose health is good, and who has a sufficient amount of rest and proper nutrition, has a greater cardiac reserve than one who has no such advantages A person who has had a sedentary, indoor occupation all his life, such as a bookkeeper, and who has had no athletic activity will have a lower cardiac reserve than one whose occupation called for considerable muscular activity, such as a truck driver or farmer. The tensile force of the heart muscle will be greater in the second group. This is illustrated in Fig. 70.

In abnormal constitutional states or in disease of the cardiovascular system, the reserve force of the heart is encroached upon and signs of failure develop on effort. The amount of effort that brings about failure depends upon the amount of reserve force the heart muscle possesses. In severe cases of cardiovascular disease the rest force of the heart may also be affected. In such cases, signs of cardiac failure are present even with the patient at rest.

Based upon the variations in the cardiac functional states in different individuals with different degrees of organic heart disease, The American Heart Association[1] adopted the following classification of the *functional capacity* of any given patient

Class I—Patients with a cardiac disorder without limitation of physical activity. Ordinary physical activity causes no discomfort.

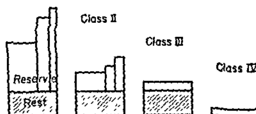


FIG 71—HEART DISEASE WITH ITS VARIOUS CLASSES OF FUNCTIONAL CAPACITY The reserve force progressively diminishes in Classes I, II and III respectively In Classes I and II, the diminution varies with the previous constitutional state In Class IV, there is no reserve force and even the rest force is diminished

Class II—Patients with a cardiac disorder with slight to moderate limitation of physical activity. Ordinary physical activity causes discomfort

Class III—Patients with a cardiac disorder with moderate to great limitation of physical activity. Less than ordinary physical activity causes discomfort

Class IV—Patients with a cardiac disorder unable to carry on any physical activity without discomfort

In the proper use of this classification it is essential that the term "ordinary" physical activity be clearly understood. Inasmuch as the reserve force of the heart, and therefore, the capacity for physical activity in normal individuals varies, what may be ordinary physical activity for a truck driver or farmer will be extraordinary for a person who has always lived a sedentary life, even though each of these individuals has a structurally normal heart In determining the classification of an individual having heart

disease we must, therefore, consider the patient's reaction to the type of activity which he customarily carried on without discomfort before he developed his heart disease The various grades of the functional capacity of the heart in disease is illustrated diagrammatically in Fig 71.

The underlying physico-chemical causes of heart failure are not entirely understood. That structural disease alone is not the cause is evidenced by the fact that in many cases of heart failure, the amount of anatomic myocardial disease is not of sufficient degree to account for the failure. Also, many cases showing marked structural disease of the heart on postmortem examination did not show failure during life It is believed that failure is provoked by an accumulation of the waste products of muscle metabolism such as lactic acid and others, associated with contraction Redfield and Medearis[2] have shown the relation of lactic acid and the development of cardiac muscle tension Excessive accumulation of waste products causes a state of fatigue and loss of tensile force of the heart muscle fibers The *result is abnormal stretching of the muscle fibers and insufficient rebounding force* In other words, there is a decrease in the mechanical efficiency of the heart muscle Starling and Visscher[3] have shown that the amount of oxygen consumed by the failing heart is increased and this increase is proportional to the degree of dilatation of the heart muscle This would indicate that although the energy liberated in the failing muscle is increased, such energy is not in the form of mechanical work.

The cardiac output in heart failure is diminished to an extent corresponding to the degree of failure In a review of the literature and in a study of their own 42 cases, Suarez and co-workers[4] found the cardiac index in heart failure to drop from the normal of 2 27 liters per square meter of body surface per minute to 1 50 liters in marked failure, with intermediate figures between, depending upon the degree of failure The systolic output per square meter of body surface varied between 35 4 cc for normal controls to as low as 19 3 cc in severe decompensation

Localization of Heart Failure

Myocardial failure may develop in both ventricles simultaneously or in either the right or left ventricle alone or predominantly, depending upon the underlying cause or causes When a given ventricle fails and does not propel the blood forward in a normal manner, dilatation of the auriculoventricular orifice and the corresponding auricle takes place as a result of stretching and stasis If the process occurs slowly over a long period of time, hypertrophy of the corresponding auricle and ventricle occurs.

Causes of Heart Failure

Simultaneous *failure of both ventricles* may occur in conditions that strain the entire heart, such as in marked, prolonged tachycardias and arrhythmias. The shortened diastolic period in such cases diminishes the

coronary blood supply and also prevents the musculature from getting sufficient rest between contractions The heart muscle thus undergoes fatigue and suffers from anoxemia and the accumulation of waste products, resulting in dilatation. The same may occur in coronary disease if it is of sufficient degree to diminish the blood supply to both ventricles, even if the rhythm is regular and the heart rate is not excessive. Also narrowing of the coronary ostii in the aorta in syphilitic or other pathologic conditions of the aortic wall in the region of the coronary orifices may produce failure Acute or subacute myocardial inflammations or infarction as well as the severe anemias, vitamin B and dietary deficiency and myxedema may produce myocardial failure. In cases of marked degree of mitral insufficiency, failure of both the left and right heart may occur, left heart failure being due to strain upon the left ventricle and right heart failure to back pressure and the resulting increase in resistance of the pulmonary circulation

Predominant *failure of the right ventricle* may occur in any condition that throws a great strain upon that ventricle due to increased resistance to the free flow of blood through the pulmonary vascular system. These are, mitral stenosis, if advanced and of long standing, some congenital heart lesions; chronic pulmonary disease, notably asthma, emphysema, pleuropulmonary fibrosis and others, and hypertension with sclerosis of the pulmonary vascular system. Sudden acute right heart failure may occur in massive acute pulmonary infarction due to embolization from venous thrombosis anywhere in the body, in the absence of any of the above conditions

Predominant *failure of the left ventricle* may occur in any condition straining that ventricle Chronic aortic valvular disease and systemic hypertension are the two outstanding causes The latter is the most frequent

In all conditions, where the underlying disease process develops slowly, the ventricle affected undergoes intermittent strain resulting in some dilatation of the muscle fibers followed by hypertrophy. Failure in such cases is usually precipitated by prolonged strain with insufficient rest, some superadded low grade infection, excitement, overeating or reactivation of the disease process that brought about the valvular or other defect. The onset of coronary sclerosis in conditions of well compensated valvular disease or in hypertension is frequently the cause of myocardial failure after 40 years of age. Hypertrophy of the muscle itself, if reaching a marked degree, even without coronary disease, may result in relative coronary insufficiency and myocardial failure The coronary supply in such cases may become inadequate because of the muscle fiber hypertrophy.

Symptoms of Heart Failure

Heart failure produces a train of symptoms and signs by which it can be recognized. These vary with the location and degree of failure.

Left Ventricular Failure

The *characteristic symptoms* of left ventricular failure are those due to respiratory embarrassment. They consist of dyspnea and orthopnea, pulmonary edema, cough, unproductive early and later with frothy sputum, asthmatic breathing or so-called cardiac asthma and Cheyne-Stokes breathing. Each of these may appear alone or in various combinations in different individuals.

In addition to these characteristic symptoms, other disturbances may occur in many cases, such as weakness, easy fatigability, digestive disturbances, palpitation, precordial discomfort or ache and in severe cases, fear of suffocation and cold clammy perspiration

Pathogenesis The characteristic respiratory symptoms are due to physiologic disturbances of the normal mechanism of respiration A short review of the mechanism of normal respiration is therefore essential for a proper understanding of the respiratory disturbance in left heart failure

Normal respiration is maintained by rhythmic stimuli coming from the respiratory center in the medulla These stimuli influence secondary centers, located mainly in the spinal cord, producing an harmonious discharge of impulses to the various muscles of respiration and resulting in normal inspiration and expiration in their proper time relationship.

According to Macleod,[5] the rhythmic stimuli sent out by the respiratory center are very weak and are greatly influenced by afferent stimuli arriving in this center from different parts of the body, particularly the lungs The impulses from the lungs reach the respiratory center mainly through the vagus which contains two kinds of afferent fibers, one stimulating inspiration and the other expiration. These affect mainly the rate of respiration Other afferent impulses arising from other parts of the body have an inhibiting or accelerating effect on respiration. For instance, swallowing, singing, micturition and defecation may have temporary inhibiting effects. Irritation of the mucous membrane of the larynx by a foreign body may excite violent expiration. The depth and rate of respiration may also be modified consciously and in various nervous disturbances apparently unconsciously, through the cerebral centers. This would explain the abnormalities in respiration in neuroses or hysteria

Besides these reflex factors, the respiratory center is also controlled by chemical substances. These normally consist of hydrogen ion concentration and the oxygen and carbon dioxide tension of the blood. The latter two are directly related to their concentration in the air of the alveolar spaces in the lungs Increased carbon dioxide tension in the arterial blood above normal will stimulate the respiratory center and produce dyspnea. Marked anoxemia or decrease in the oxygen content as well as acidosis or

increase in the H ion concentration will also produce the same effects. The reverse is true A marked increase in the oxygen tension as well as a decrease in the CO_2 tension and in the pH concentration of the blood results in apnea.

In left heart failure all these factors enter into the production of respiratory disturbances. There is distention of the arteriolo-capillary-venular radicles of the pulmonary vascular tree due to increased pressure in the *pulmonary veins* caused by the failing left ventricle This distention results in encroachment on the alveolar spaces The respiratory distensibility of the lungs and therefore its vital capacity are thus diminished. The extent of such diminution depends upon the degree of pulmonary vascular engorgement and this in turn upon the degree of left heart failure If the process is extensive, exudation in the alveolar spaces takes place, resulting in pulmonary edema Capillary rhexis may occur due to this distention which together with the edema results in frothy, blood-tinged sputum.

Due to the pulmonary stasis, the normal exchange of oxygen and carbon dioxide between the alveolar air and the blood in the pulmonary capillaries is interfered with Also because of an insufficient forward propulsion of the blood by the left ventricle, the various tissues of the body suffer to some extent from improper nutrition and an insufficient oxygen supply. There is, as a result, an accumulation in the tissues of CO_2 and some of the products of improper metabolism, notably lactic acid. The respiratory center being most susceptible to these products is thus stimulated to greater activity.

Distention of the pulmonary vascular radicals stimulates the vagal afferent fibers, resulting in a greater flow of impulses to the respiratory center and thus in greater activity of that center. Likewise, impulses from the higher cerebral region resulting from apprehension increase the activity of the respiratory center, accentuating the dyspnea, pulmonary edema and other respiratory disturbances The psychic effect is very apparent to anyone who has experience with these cases The suddenness of onset of alarming respiratory symptoms when the examining physician expresses anxiety or alarm in the presence of the patient with moderate dyspnea is often a striking phenomenon. Recent work by Luisada and Sarnoff[6] suggests that even pulmonary edema may be due to a reflex nervous factor affecting the permeability of the capillaries They believe that the afferent impulses originate in the carotid sinus region or in the distended left ventricle.

Dyspnea may develop on effort or spontaneously.

Effort Dyspnea: This varies in degree from mild shortness of breath coming on after extreme exertion to severe attacks coming on after the slightest exertion, depending upon the degree of left ventricular failure. In very severe cases, there is marked dyspnea even at rest. Here, the mere work of the metabolic activities of the body entail strain on the heart. In such

cases, the patient must sit up in order to be able to catch his breath—a condition known as *orthopnea.* If care is taken to rule out other conditions causing dyspnea, the amount of dyspnea produced by a given effort may be used as a measure of the extent of left heart failure.

Paroxysmal Dyspnea: Of great interest are those cases where dyspnea occurs *spontaneously* in paroxysms, usually at night, a condition known as *paroxysmal nocturnal dyspnea* These cases may be relatively free from symptoms during the day and may even be able to carry on moderate activity without much discomfort

The attack comes on abruptly, usually in mild, transient form, lasting a very short time. Often, however, it appears with severe intensity, awaking the patient from sleep. It may be associated with a marked choking and suffocating sensation or severe precordial oppression, marked apprehension and anxiety, with a sensation of impending death The patient is compelled to sit up and gasp for air. The whole body may be covered with cold clammy perspiration and there may be marked pallor associated with some cyanotic tinge. The breathing often resembles that of allergic asthma and the term *cardiac asthma* is therefore often used to describe this condition Pulmonary edema frequently supervenes with cough and expectoration of frothy, blood tinged sputum The similarity of the respiratory pattern in allergic asthma and paroxysmal dyspnea was demonstrated by Heyer.[7]

The abruptness and apparent spontaneity of the onset of the attack speaks for a sudden overwhelming stimulation or irritation of the respiratory center which is already overstimulated by the pulmonary stasis Why it occurs most often at night when the patient is at rest, is hard to explain. It is probably due to a greater accumulation of the products of metabolism in the respiratory center owing to increased slowing of the circulation during sleep The absence of mental inhibition of the respiratory center during sleep that occurs in waking hours may be another factor. A third possible mechanism is an increased shift of fluid from the periphery to the lungs with the assumption of the recumbent posture Disturbances in other parts of the body may, in some cases, serve as trigger mechanisms, overwhelming the respiratory center, inasmuch as dreams, abdominal distention, overeating at bedtime, a coughing spell and other factors have apparently acted as precipitating causes of the onset of attacks.

There is definite similarity in many cases of the abruptness of onset of paroxysmal dyspnea and spontaneous agina pectoris. As Pratt[8] has pointed out, the same attack may, at times, be regarded by one observer as paroxysmal cardiac dyspnea with pain and by another as angina pectoris with dyspnea.

Like bronchial asthma, cardiac asthma is undoubtedly caused by narrowing of the bronchiolar lumena due to reflex effect induced by circulatory

stasis. There may also be a certain amount of exudation and plugging of the smaller bronchial radicals. It is very likely that in all these cases some degree of chronic bronchitis and in occasional cases, bronchiectasis may be present as a background which help precipitate such attacks in an acute congestive state Similar attacks are often observed also in pulmonary stasis due to mitral stenosis, where sudden, prolonged acceleration of the heart which acutely overloads the pulmonary vascular system is the precipitating cause of acute cardiac asthma Here also, chronic bronchitis is often present as an underlying cause. In fact, both prolonged left heart failure and mitral stenosis which are associated with pulmonary stasis and turgescence of the mucous membrane of the bronchial tree may lead to chronic bronchitis and emphysema Many of these cases have in addition, an allergic background and suffer also from allergic asthma in addition to cardiac asthma

The differential diagnosis between cardiac and allergic asthma is of importance. Allergic asthma is a very disturbing and debilitating disease but the prognosis is, in the majority of cases, good Most sufferers may live useful lives and are comparatively free from symptoms for long periods Cardiac asthma, on the other hand, is a very serious condition and death may occur in some cases, suddenly Therapeutically, likewise, the two conditions are different. Allergic asthma often responds quickly to adrenalin, but when given in cardiac asthma it may occasionally produce death, although even here it may, at times, be of help On the other hand, digitalis may be of great value in cardiac asthma but will not have any effect on bronchial asthma

The differential diagnosis is based on the facts that in allergic asthma, symptoms usually appear early in life and there is no demonstrable evidence of organic heart disease There are also, as a rule, no moist, inspiratory rales at the bases of the lungs which are often found in left heart failure. In most cases, there is a history of allergy in the family and the patient often presents other allergic manifestations, such as urticaria, angioneurotic edema and so on The mucous secretions from the nose as well as sputum may show many eosinophile cells and Charcot-Leyden crystals are present in the sputum The noninfectious type may present an eosinophilia. The skin sensitivity tests are, of course, valuable in the pure allergic type but not in the type of bronchial asthma associated with chronic pulmonary infection.

Cheyne Stokes Respiration· This type of breathing, often observed in left heart failure, especially in the elderly arteriosclerotic type, is characterized by periods of apnea followed by hyperpnea The hyperpnea usually develops slowly, reaches a peak and subsides slowly. In most cases, it develops during sleep but in severe cases of heart failure, i ay be present in a marked degree during waking hours.

The disturbance is observed also in other conditions than left heart failure, such as increased intracranial pressure, due to any cause, local circulatory disease of the respiratory center, meningitis, uremia and diabetic acidosis.

The underlying mechanism is not known. Pembrey and Allen[9] attribute it to diminished excitability of the respiratory center due to deficient blood supply. Prolonged apnea results in an excessive accumulation of CO_2 which reaches a level sufficiently high to stimulate the depressed center The resulting hyperpnea reduces the CO_2 in the blood to a level insufficient for the center to respond, resulting again in apnea Thus, the process recurs This view is not universally accepted Some believe that the condition is caused by periodic alterations in the excitability of the respiratory center.

Differentiation of Cardiac from Other Forms of Dyspnea Dyspnea due to cardiac disease may be simulated by other conditions which must be borne in mind in our differential diagnosis Among them are mechanical factors, increased metabolic activity of the body, interference with the proper oxygenation of the blood or proper transportation of oxygen by the blood *and neurogenic disturbances*

Mechanical factors such as local tracheal or laryngeal obstruction by new growth or foreign body or obstruction of the trachea or bronchi by an aortic aneurysm or mediastinal tumor may produce dyspnea. These conditions may be easily differentiated by examination.

Obesity, involving mainly the abdominal region, may produce some dyspnea by raising the diaphragm and interfering with its free excursion, thus diminishing the vital capacity of the lungs Thoracic deformity, congenital or acquired, may also produce the same effects In both, obesity and thoracic deformity, dyspnea is of no importance unless the heart is involved. In rare cases of severe chest deformity resulting in distortion and displacement of the heart, cardiac hypertrophy and failure may occur. In the absence of cardiac abnormalities, however, some dyspnea that may be present should not be attributed to heart disease.

Increased metabolic activity of the body such as occurs under physical strain, in thyrotoxicosis and in febrile states, may be associated with some degree of dyspnea even in the absence of left ventricular failure. The dyspnea will last only as long as the increased metabolic state continues

Interference with proper airation resulting in an accumulation of CO_2 in the blood may occur in all forms of acute or chronic pulmonary disease and will result in dyspnea. The more common pulmonary diseases are the various forms of pneumonitis, tuberculosis, primary and metastatic carcinomatosis and other tumors of the lung, pneumonoconiosis, chronic pulmonary fibrosis, chronic bronchitis, massive bronchiectasis, emphysema and hydrothorax due to infections or malignancy. In many, if not all of these cases, dyspnea is

probably partly due also to reflex stimulation of the respiratory center by the pulmonary disease.

Improper transportation of oxygen by the blood may occur in the various anemias and leukemias, where there is marked diminution in the number of red blood cells as well as in severe hemorrhage, reducing the total volume of blood It may also be observed in severe polycythemia

Psychoneurotic disturbances are very frequent causes of abnormalities in respiration which may superficially simulate cardiac dyspnea The respiratory disturbances may be in the form of marked increase in the rate of respiration or there may be a feeling of distress associated with breathing Often there is a peculiar sighing with respiration In all these cases, there is no actual dyspnea and the vital capacity may be normal In hysteria, the patient may exhibit all kinds of forced respiration

The author recently observed a female, 46 years old, who was subject to severe attacks of peculiar gasping breathing with complaints of choking, occurring mainly in the middle of the night She had no demonstrable organic heart disease and there were no congestive rales at the bases or increase in the vascular markings of the lungs, fluoroscopically Her vital capacity was normal The breathing was not that of prolonged expiration usually seen in paroxysmal nocturnal dyspnea but more of a type of forceful inspiration She was introspective and lacked the sympathy of her family which she evidently sought The disturbed breathing was probably a conscious or subconscious expression of desire for attention

In most cases of respiratory disturbances, not due to cardiac disease, the differential diagnosis from cardiac dyspnea can be readily made by careful physical and roentgenologic examinations of the lungs The presence of cardiac enlargement, valvular disease, hypertension, important abnormalities in the rate and rhythm of the heart, abnormalities in sounds, a gallop rhythm, congestive rales at the bases of the lungs, diminished vital capacity of the lungs and accentuated pulmonic second sound—would speak for dyspnea as being of cardiac origin It must be borne in mind, however, that dyspnea may often be caused by a combination of factors, heart disease being one of them

Heart disease itself may produce or increase existing dyspnea by mechanical means, such as pressure on the lungs, by massive pericardial effusion or by an extremely large left auricle Massive pleural effusion may produce the same effect

Right Heart Failure

The primary symptoms of right heart failure are systemic edema, cyanosis and more or less distention of the peripheral veins, especially those of the neck, due to increased venous pressure. The veins may show pulsation The

secondary symptoms are due to stasis and edema of the internal organs, to be described shortly.

Systemic Edema

Manifestations. In the very early stages edema may be occult, without gross detectable evidence. It may be demonstrated by gradual increase in weight, if the patient is weighed periodically and by some diminution in the urinary output in relation to fluid intake In later stages edema may be detected by peripheral swelling The characteristic of such swelling is that it follows the law of gravity Thus, in ambulatory patients, there will be noted towards evening, some edema of the ankles which disappears after a night's rest The amount of edema is the same in both lower extremities unless there is an additional factor of local venous obstruction in one extremity, when the edema there will be greater As time goes on, if heart failure is uncontrolled, the edema increases and may not fully subside after a night's rest It soon extends to the scrotum, the buttocks, the back and the rest of the body. The face is usually spared, although in severe cases, the face may also be somewhat involved In bedridden patients, the swelling usually collects first in the scrotum and on the side of the body on which the patient sleeps

The edema of cardiac failure pits readily on pressure and the pitting quickly disappears The color of the skin may be pale but is often somewhat dusky In long standing edema, the skin usually becomes thickened, hardened, more or less red and glossy and does not readily pit on pressure

Edema of the internal organs may be localized predominantly in one organ, notably the liver but in severe generalized edema, known as *anasarca*, all organs are affected in a greater or less degree.

The liver becomes markedly engorged and its edge may extend down to the pelvis. If the swelling develops rapidly, marked pain and tenderness occur due to sudden stretching of Glisson's capsule and if ascites is present so that the liver edge cannot be felt, the condition may be mistaken for acute cholecystitis In long standing congestion, cirrhosis of the liver occurs and jaundice may develop The jaundice usually affects only the nonedematous areas of the skin, as pointed out by Meakins [10]

Due to stasis and congestion of the gastro-intestinal tract, nausea and vomiting may occur and in severe cases, bloody stools may be passed Massive ascites, hydrothorax and hemopericardium may occur in very severe cases.

Due to congestion of the kidney and to general stasis, the urine in severe cases is scant, of high specific gravity and highly colored. It may contain albumin, casts and blood cells. Stasis and edema of the brain, if marked,

will result in mental torpor, drowsiness, lack of interest, stuporous state, delirium and coma.

Mechanism: As described in Chapter IV, the interchange of fluids between the capillary system and the tissue spaces, as first elucidated by Starling, depends primarily upon the physical forces of colloidal osmotic pressure and the hydrostatic pressure of the blood in the capillaries. If the hydrostatic pressure is greater than the colloidal osmotic pressure, the fluids will flow from the capillaries into the tissue spaces If less, fluids will flow from the tissue spaces back to the capillaries

It is assumed that the production of edema is due to increased venous pressure which is propagated to the venular radicals and to the capillary tree. The hydrostatic pressure in the capillaries is thus increased above the colloidal osmotic pressure This results in a greater escape of fluids into the tissue spaces. There is also the additional factor in this condition of stretching and possible injury of the capillary wall, due to the capillary hypertension, with the escape of some of the colloids into the tissues, thus further lowering the colloidal osmotic pressure in the capillaries. That blood plasma is often diminished in patients with cardiac insufficiency was first shown by Epstein [11]

Recently, Warren and Stead[12] brought forward some evidence which tends to refute the theory that increase in venous pressure is the primary cause of edema. In a study of two cases, they found that increase in body weight which indicates an accumulation of fluid, occurs before any increase in venous pressure could be demonstrated There was, at the same time, an increase in the circulating blood volume, and a hemodilution The latter was shown by a fall in the hematocrit reading and in the diminished concentration of the plasma protein. They, therefore, conclude that edema in chronic congestive failure is caused by inability of the kidneys to excrete salt and water due to decreased cardiac output, and not to engorgement of the kidneys from increased venous pressure. The retention in the blood of the salt and water produces the increase in plasma volume resulting in a decrease in the concentration of plasma protein This, in turn, stimulates the production of more plasma proteins resulting in an increase in the total amount of circulating protein, so that the osmotic pressure of the plasma protein is not markedly lowered. The rise in venous pressure occurs later and is caused by the increase in the blood volume and extracellular fluid volume They admit, however, that a local increase in venous pressure is important in the production of local edema.

Merrill,[13] likewise, brought forward some evidence showing that reduction of blood flow through the kidneys in congestive failure bears no relation to venous pressure, but is related to a reduced cardiac output.

Reichsman and Grant[14] disagree with the views of Warren and Stead. In

three cases which they studied, the venous pressure was elevated before there was an increase in body weight. Landis and co-workers[15] also disagree with Warren and Stead They consider muscular activity as a contributing factor in the elevation of venous pressure in cardiac failure. The two cases studied by Warren and Stead were in the resting state

The underlying mechanism of congestive failure certainly requires further investigation Neither the so-called "forward" nor the "backward" theory of heart failure explains all the phenomena observed There are, undoubtedly a great many disturbances in the hormonic, nervous and physico-chemical control of capillary filtration, as described in Chapter III, which are at least partly responsible

Pleural Effusion Due To Heart Failure· This most frequently occurs in the right pleural cavity, and if both are involved, there is a greater amount in the right In the various reported cases in the literature about 60 to 80 per cent occur in the right chest

The reason for the greater frequency of right hydrothorax than left hydrothorax in cardiac failure is not clear The old theory, that pressure on the root of the right lung or azygus vein by an enlarged right auricle is a cause, has been questioned Fetterhoff and Landis[16] felt that transudation of fluid into the pleural cavity occurred through the visceral layer of the pleura and the condition was, therefore, due to pulmonary, rather than systemic stasis Dock[17] showed that anatomic and hydrostatic factors relating to the flow of blood from the pulmonary veins to the left auricle favored the predominance of right over left hydrothorax This is augmented by the right lateral recumbent posture which these patients prefer. Drinker[18] believes that both, simple pulmonary edema as well as marked exudation, depend more upon changes in the permeability of the lung capillaries than upon the pressure relations in the pulmonary circulation The right lung being larger than the left, has a greater surface area for exudation

Clinical Differentiation Between Cardiac and Other Forms of Edema. Edema may be caused by a variety of conditions besides heart disease That caused by local venous obstruction, drug allergy and angioneurotic edema which is usually asymetrical, should not be difficult to differentiate from cardiac edema

Of the *symmetrical* type of edema, that caused by *glomerulonephritis* and *nephrosis* may simulate cardiac edema. In nephritis, however, the edema appears first on the face and does not follow the laws of gravity. In nephrosis, the edema is softer than in cardiac edema, and pitting does not disappear as readily. Also, the color of the skin over the edematous area is much whiter.

Obstruction of the superior vena cava or its main branches will result in edema

of the neck, face and arms, but not of the lower extremities. Similar obstruction of the inferior vena cava will result in marked edema of the legs and lower part of the trunk, but not of the upper part.

The severe anemias, avitaminosis and starvation may produce general edema. The difficulty in the differential diagnosis here lies, at times, in the fact that the heart may temporarily show considerable abnormalities in such conditions A blood study in the former and a nutritional history in the latter will help in the differential diagnosis.

In *myxedema* the swelling may have some resemblance to cardiac edema. The differentiation may be particularly difficult if some degree of cardiac edema is also present Ordinarily, the edema in pure myxedema does not pit on pressure, although some pitting may be observed in an occasional case. The thickened speech, diminished mental and physical power, the bloated, expressionless face, thick tongue and pallid color should offer no difficulty in diagnosis A basal metabolic rate determination will further help in the diagnosis

Edema of the lower part of the body, ascites, liver enlargement and hydrothorax caused by congestive failure must always be differentiated from a similar condition caused by *malignancy* The author has seen several instances of misdiagnosis This is especially true where cardiovascular disease is also present, besides malignancy

A good example is a male, 52 years old who gave a history of progressive shortness of breath, cough, weakness, some swelling of the abdomen and the lower extremities of six months' duration He was treated for cardiac decompensation with digitalis and mercurial diuretics but the symptoms progressed When the author first examined him, six months after the onset of symptoms, he presented left massive hydrothorax The right lung showed hyperesonance, exaggerated breathing and a few congestive rales but there was no demonstrable fluid in the right chest cavity The heart sounds were diminished in intensity at the apex due to the hydrothorax but there was no gallop rhythm There was a loud rough systolic murmur at the aortic region with a large area of transmission The liver was markedly enlarged and was irregular. There were considerable ascites, and edema of both lower extremities, more on the left The author's impression was that he had calcific aortic stenosis but the heart was not in congestive failure All the signs and symptoms were attributed to left pulmonary malignancy, probably bronchogenic, with metastases to the liver and abdominal lymphatics. Aspiration of the left chest yielded a sero-sanguinous fluid showing many tumor cells He died two months later [illegible]

hypertrophy, but no cardiac dilatation

Cyanosis

There are two principle causes of cyanosis in cardiovascular disease. One is the existence of an arterio-venous shunt with conditions favoring the flow of a considerable amount of venous blood into the arterial system. The other is circulatory failure. The former is observed in some forms of congenital heart disease to be described in Chapter XXVII.

Cyanosis due to circulatory failure may occur to some extent in left heart failure and in shock. It is, however, most pronounced in the presence of right heart failure.

Pathogenesis. The condition is caused by a reduction in the amount of oxyhemoglobin in the blood.

According to Lundsgaard and Van Slyke,[19] the oxygen capacity of the blood under normal conditions is about 20 cc. per 100 cc. of blood or 20 volumes per cent. The usual arterial blood, however, shows only 95 per cent saturation or 19 volumes per cent, that is, 1 per cent unsaturation. This oxygen content is reduced in the capillaries in various regions of the body according to the needs of the given tissues. A sample of venous blood, representing the average mixture returning from all capillary beds, may show only 14 per cent saturation of oxygen or 6 per cent unsaturation. The average capillary unsaturation would, therefore, normally be perhaps in the neighborhood of about $\frac{1+6}{2}$ or 3.5 per cent. Lundsgaard and Van Slyke found that cyanosis appears when the mean capillary unsaturation is 6 to 7 per cent. Inasmuch as 1 cc. of oxygen combines with 0.75 grams of hemoglobin, cyanosis will appear when there is about 5 grams of reduced hemoglobin per 100 cc. of blood.

Unsaturation of hemoglobin with oxygen and therefore the appearance of cyanosis is frequently observed in acute or chronic pulmonary disease in the absence of heart failure. The arterial blood in such cases will show a saturation less than 19 volumes per cent. In heart failure, the intrapulmonic hypertension and associated pulmonary stasis is one factor which operates in the production of cyanosis. Another factor is the systemic venous stasis producing widespread capillary distention and retardation of blood flow. This slowing of the blood stream results in a greater reduction of the oxyhemoglobin in the tissues.

Manifestations: The ability to detect cyanosis varies with the acumen of different observers, as shown by Comroe and Botelho.[20] They found that various grades of arterial anoxemia may not be recognized by many physicians and they feel that the visual impressions of cyanosis are unreliable. The detection of cyanosis is also dependent on various modifying states of the patient, as shown by Lundsgaard and Van Slyke. Some of these are

the thickness, color and opacity of the skin or membrane overlying the capillaries and the number and length of blood-filled capillaries in a given surface area as well as the state of vascular constriction in that area. For these reasons, cyanosis, when not marked, may often best be seen in the tips of fingers and toes, especially in the nail beds, lips, tips of the nose, cheeks and ears. It is also often seen best in the mucous membrane of the mouth and in the conjunctiva. In the Negro, these are the only places, of course, where cyanosis may be detected

In more advanced cases, the entire body surface may show more or less cyanosis Often the cyanosis may assume a mottled appearance. This is seen especially in the lower extremities.

The cyanotic hue may vary in different conditions from pale bluish to dark blue depending upon the degree of cyanosis. In peripheral vascular failure the color is often ashen In the presence of jaundice, cyanosis assumes a bluish-yellow color.

Cyanosis Not of Cardiac Origin We occasionally observe considerable cyanosis in the absence of demonstrable cardiac, respiratory or marked general peripheral vascular failure One of these conditions is the erythrosis of polycythemia vera. The color here, however, is brick red rather than cyanotic, due to overdistention of the arteriolo-capillary radicals

Another condition is the cyanosis due to vasomotor instability, seen especially in neurocirculatory disturbances Here the hands particularly are apt to show marked blueness, coldness and sweat. The condition is due to local arteriolo-capillary-venular stasis

A third and very serious condition is the conversion of oxyhemoglobin into methemoglobin by such drugs as acetanilid, bismuth subcarbonate, chlorates, nitroglycerine and other nitrites, aniline dyes and perhaps also some toxins. This may occur in susceptible individuals even if comparatively small doses of these drugs are taken The iron of the hemoglobin is converted to a ferric state, losing its capacity to combine with oxygen The condition, if marked, may be rapidly fatal It is essential to bear this condition in mind in patients who use nitroglycerine or other of the above drugs and among workers in the aniline dye industry

Symptoms of Combined Right and Left Heart Failure

When right heart failure follows prolonged left heart failure, the severe dyspnea present before often greatly diminishes, due to insufficient propelling force of the right ventricle which diminishes the flow of blood towards the lungs Pulmonary engorgement thus decreases.

Simultaneous failure of both ventricles results in a combination of symptoms, enumerated under the failure of each ventricle separately. Although dyspnea may not be very conspicuous, cyanosis is usually marked. Also

peripheral edema, liver enlargement, and other signs of systemic stasis are prominant

Aids in the Diagnosis of Heart Failure

Cases of heart failure with evident clinical signs and symptoms are usually readily recognizeable and can be differentiated from other conditions. When in doubt, or where the condition is in its early phases, we may have to resort to other aids in diagnosis Of these, the simplest are the determination of the vital capacity, the venous pressure and the circulation time

Vital Capacity Determination This is based on the fact that in pulmonary engorgement due to left heart failure, the total volume of air which can be exhaled by maximum expiration after a maximum inspiration, that is, the *vital capacity* of the lungs, is diminished

In normal individuals the vital capacity varies with sex, muscular development and size of the person The predicted value in any case, according to West,[21] may be determined from the surface area of the body which is given in a convenient chart by DuBois and DuBois It may also be determined from the height alone The vital capacity in cubic centimeters should be equivalent approximately to the surface area in square centimeters multiplied by 2 5 in men, 2 in women and 2 8 in athletes If the height only is used, the vital capacity in cubic centimeters will be approximately the same as the height in centimeters multiplied by 25 in men, 20 in women and 29 in athletes In children, Edwards and Wilson[22] found the average vital capacity to be about 15 5 cc per centimeter of height

Normally, the vital capacity shows a progressive diminution with advancing age after fifty years It also varies considerably with the habitus of the individual and with practice in deep breathing A vital capacity of less than 15 per cent below the estimated figure for the given individual may therefore be considered to be within normal limits in most cases.

In left heart failure, the vital capacity is greatly reduced. The amount of reduction is proportionate to the degree of pulmonary congestion and therefore to the degree of failure

Inasmuch as severe pulmonary disease, such as pulmonary fibrosis, massive tuberculosis, emphysema and others, also reduces the vital capacity, its value as a test of left heart failure is greatly limited.

Venous Pressure Studies· This is of great value in determination of right heart failure The method of study and its limitations have been covered in Chapter IX

The Determination of the Circulation Time The term "circulation time" is used to designate the time it takes for blood to pass from one part of the cardiovascular system to another. *It is an approximate measure of the veloc-*

ity of blood flow. Inasmuch as the velocity of blood flow is the resultant primarily of the force of ventricular contraction, slowing of the circulation time may indicate more or less failure of one or the other ventricle, depending upon where the slowing occurs It must be realized, however, that this method is merely a rough estimation of the circulatory velocity. This will be understood from a consideration of the physiologic mechanism of the circulation in Chapter IV.

The methods used to determine the circulation time consist of injecting some material in one of the veins, preferably the antecubital and detecting it in the arterial system in another part of the body or in the antecubital vein in the other arm The method of its detection is based upon the subjective or objective effects the material produces. The period elapsing from the moment of injection to its detection is spoken of as the circulation time.

Various substances have been used clinically in studying the circulation time, the more frequent of which are radium C by Blumgart,[23] histamine by Weiss, Robb and Blumgart,[24] decholine by Winternitz and co-workers,[25] sodium cyanide by Robb and Weiss,[26] saccharin by Fishberg and co-workers,[27] ether by Hitzig[28] and amyl nitrite by Gross [29] The end point of the circulation time, as determined by any of these products, depends upon the physiologic effect of the given product. This may be subjective or objective. Thus, the end point of radium C is determined, after injection, by a detecting device on its appearance in the heart or in peripheral parts of the body Histamine arrival in the vessels of the face is evidenced by flushing of the face and by a metallic taste in the mouth It is thus an objective and subjective method Decholin is detected by its bitter taste, sodium cyanide by deepening of respiration, saccharin by its sweet taste, ether by its smell and amyl nitrite by flushing of the face.

It will be observed that some of the products used are detected as soon as they enter the lung and before they reach the systemic arteries They thus roughly measure the circulation time between the vein, through the right heart to the capillary system of the pulmonary circulation. Other products are detected after they reach the systemic capillary system Still others such as amyl nitrite measure the circulation time between the lung and the vessels of the face

It must be understood that in the use of substances which depend upon their action on the subjective sensations of the patient, error may arise from variability in the individual sensitivity and alertness of the subject. The psychologic reaction time is, in most cases, an unknown quantity and may affect the estimation of the circulation time This is true especially in more or less stuporous and toxic states

The author usually uses the saccharin and ether methods employed by Fishberg and co-workers For the saccharin time 2 5 grams of soluble sac-

charin are dissolved by heating in 2 cc of sterile distilled water A 19 gage needle is used and the injection is made in an antecubital vein as rapidly as possible. The time between the injection and the detection of a sweet taste *is recorded with a stop watch Normally, this arm-to-tongue time varies* between 9 and 16 seconds For the arm-to-lung time we inject 5 minims of ether mixed with an equal amount of physiologic saline solution in the same vein and determine the time it takes for the smell of ether to be detected Normally, this time varies between 5 to 8 seconds

In right heart failure, the arm-to-lung time is prolonged, the prolongation corresponding to the degree of failure. In left heart failure, the arm-to-tongue time is prolonged It is advisable to determine the arm-to-tongue time first If normal, there is no need of determining the arm-to-lung time. If the arm-to-tongue time is prolonged, it may be due either to combined right and left heart failure or to left heart failure alone If the arm-to-lung time in such cases is normal, it would indicate that the prolonged arm-to-tongue time is due to isolated left heart failure.

Recently, Nathanson and Elek[30] have shown in a series of 70 cases of cardiac enlargement without failure that more than half had a circulation time longer than 20 seconds The greater the cardiac enlargement the longer the circulation time. Relatively greater prolongation occurs in mitral disease The prolongation in the circulation time in cardiac enlargement is probably due to greater dilution of the test substance in the increased residual *blood volume of the dilated chambers and in the pulmonary vascular system*

Complications and Sequellae of Heart Failure

The most important complication of *left heart failure* and one of the most frequent immediate causes of death is bronchopneumonia Another complication is its interference with the coronary blood supply which predisposes to further degenerative changes of the heart.

In *right heart failure* chronic stasis in the portal circulation and cirrhosis of the liver may develop, as said before Prolonged stasis will also result in chronic gastritis, intestinal disturbances, hemorrhoids, splenic enlargement and renal insufficiency. Thrombosis may occur in any of the veins of the body and may serve as pulmonary emboli Intra-auricular thrombosis may also develop The edematous skin may become susceptible to infection and ulcerations.

Brain complications may result in hallucinations, illusions and other maniacal symptoms as well as coma and convulsions The psychic disturbances of the patient are often very trying on the family, the nurse and the physician. They are usually of the depressive type and they often suffer from delusions of persecution Occasionally, the attacks are aggravated by the excessive *use of diuretic drugs*

The direct and contributing causes of death in congestive heart failure are the failure itself, pulmonary embolization and infarction, pneumonia, cerebral vascular accidents, coronary occlusion, uremia and rarely bacterial endocarditis. The frequency of occurrence of each of these factors varies with the underlying heart disease which results in congestive failure. As pointed out by Williams and Rainey[31] the incidence of death due to congestive failure itself and its immediate complications such as vascular thrombosis and embolization has diminished in recent years due to more frequent and efficient use of the mercurial diuretics. On the other hand, death due to complicating pneumonia and uremia has correspondingly increased.

TREATMENT OF HEART FAILURE

In treating a patient with heart disease, it should be our aim to attempt to prevent the onset of heart failure. If failure begins to appear, appropriate measures should be taken to retard or stop its progress. If the patient first comes under observation during an acute attack of failure, which threatens his life, urgent therapy is called for, and more stringent measures must be taken to prevent it from recurring in the future

To fulfill these therapeutic requirements effectively, it is essential to understand fully the functional capacity of the individual patient's heart and to use more or less standardized therapeutic procedures. The functional classification mentioned in the early part of this chapter and the following *therapeutic classification* adopted by the American Heart Association[1] may be used as guides in accomplishing these aims

Therapeutic Classification This consists of five classes as follows:

Class A—Patients with a cardiac disorder whose ordinary physical activity needs no restriction

Class B—Patients with a cardiac disorder whose ordinary physical activity needs no restriction but who should be advised against unusually severe or competitive efforts.

Class C—Patients with a cardiac disorder whose ordinary physical activity should be moderately restricted, and whose more strenuous habitual efforts should be discontinued.

Class D—Patients with a cardiac disorder whose ordinary physical activity should be markedly restricted.

Class E—Patients with a cardiac disorder who should be at complete rest or confined to bed

Criteria For Classification and Management To determine the classification of a given patient, his reactions to a given amount of physical activity are used as criteria Various tests have been used in determining the functional capacity of the heart, but the best test is the reaction of the patient

to a given amount of work or effort in his daily life This should be investigated very carefully by proper questioning of the patient An individual with a heart disorder who can carry on his day's work without discomfort should not be deprived of his normal activities no matter what the heart lesion may be In fact, for psychologic, as well as for economic reasons, he should be encouraged to pursue his normal activities, and even to engage in some forms of athletics to which he is accustomed. It is essential, of course, to have him under careful supervision and check-up from time to time.

If the cardiac functional state is impaired, as evidenced by the symptoms and signs described before, the degree of impairment must be determined and proper advice be given as to the type of work and the number of hours per day to give to such work as well as the amount of rest the patient is to have These should be measured by the degree of functional impairment If the symptoms and signs indicate the presence of a considerable degree of such impairment, it is always best to be on the safe side and to limit the amount of work and other activities to a degree less than the patient thinks he can carry on

The onset of detectable edema, or moderate to severe dyspnea on ordinary activity to which the patient was accustomed and which he could carry on before without discomfort, calls for temporary bed rest The length of time such bed rest is to be had depends upon the rapidity of the disappearance of the edema In the early phases, edema of the ankles usually appears toward evening, and after a night's rest it subsides The same may be true of dyspnea In such cases several days of bed rest will help restore the cardiac reserve and the patient may again be able to do work with restriction If auricular fibrillation is present, digitalis should be used in addition to bed rest, as described in Chapter VII. This drug may also be used advantageously at this stage, even in the absence of auricular fibrillation, especially if the heart rate is abnormally fast

Individuals who reach this stage of failure should not be allowed to resume the same type of work as they have done before, if it is of a strenuous nature, or the same number of hours of work if not very strenuous This modification of the work habits should last as long as there is any possibility that the patient may relapse into failure In some cases the change to lighter work and the diminished number of working hours should be permanent Some sedentary occupation, not requiring too many muscular movements may be necessary The type of work to be allowed must be determined by a careful follow-up of the individual case.

The patient must also be advised to have a greater amount of rest and sleep than he had before any signs of congestive failure developed. He must avoid staying up late at night whether for pleasure or business Sexual

relations should be limited to a minimum. Such physical activity as sw ming, tennis, handball, cycling and the like should be prohibited. Go moderation may be allowed on a straight golf course, if a follow-up of case shows no ill effects on the cardiac functional state. Frequent vacat are desirable It is essential, however, that high altitudes of 2500 fee more be strictly avoided Lower altitudes of 1500 feet or less are defin safer. The air of high altitudes has a lesser percentage of oxygen lower altitudes, and this calls forth compensatory bodily reactions suc an acceleration of the heart and an increase in the number of blood both of which are injurious in cardiac disease with a tendency to decom sation. The higher the altitude, the more the decrease in the oxygen centage and the greater the need for these compensatory bodily react

If body weight is excessive its reduction is essential This should b complished by careful dieting and not by drugs, steam baths or sweat nets. A diminished intake of fats and carbohydrates may be effecti *most cases*

Inasmuch as in some cases the precipitating cause of failure may be infection, especially of the respiratory tract, it is essential that patients a tendency to congestive failure avoid all forms of infections. Proper c ing in cold weather and the avoidance of contact with individuals suff from colds, pneumonia or other infections, and also the avoidance of exp to inclement weather are essential.

All mental and nervous irritation and excitement must be strictly av because of their accelerating effect on the heart and their tendency to duce the arrhythmias Tobacco and the excessive use of coffee and tea produce the same effects and must therefore be used cautiously.

In spite of all the precautions we may take in an attempt to preve attack of severe congestive failure, a great many cases with cardiac d will develop such failure sooner or later The reason is that many pat either can not or will not fully follow the necessary precautions Als many other cases there are certain unknown factors which precipitate at and which, therefore, can not be avoided Furthermore, in most case underlying etiologic factors such as hypertension, arteriosclerosis and o which cause the heart disease are progressive and can not be arreste our present methods of management. Hence, sooner or later enough a myocardial damage may be produced to precipitate attacks of cardiac fa in such cases in spite of the known preventive measures used

Management of Severe Heart Failure

The management of severe heart failure varies with the urgency of s toms and signs These are directly related with the predominant fo heart failure, whether right or left. In predominant right heart failu

physical suffering of the patient is not nearly as marked as in predominant left heart failure, and the immediate urgency for active therapy is not as great unless certain complications develop

The therapeutic indications in all forms of severe heart failure consist of rest, careful feeding, and the use of digitalis, diuretics and oxygen. Often, other medication is called for to improve the general constitutional state of the patient, and to overcome an associated infection, or other complication, if present

Rest Therapy This should include complete physical rest and mental relaxation The object is to diminish the metabolic activities of the body to a minimum, and thus decrease the circulatory requirements. In some of the milder cases, prolonged rest, properly carried out, will in itself relieve the decompensation without the use of drugs

The patient is to be propped up in bed, supported by a well-cushioned back rest A properly adjustable hospital bed is best suited for that purpose It should be so arranged as to prevent the patient from sliding down by raising the portion of the bed under his knees, and thus supporting the thighs A back rest and thigh support may, however, be arranged in an ordinary bed If orthopnea is severe, it is often better to have the patient sit in a reclining chair adapted with arm rests and well padded with cushions.

The enviroment should be cheerful, the room well aerated, with sufficient sunshine, proper temperature ranging between 65 and 68° F and normal humidity Sufficient bedclothes should be had, but overwarming of the body and excessive perspiration must be avoided

A well trained, tactful and intelligent nurse should be employed, one who understands the psychology of a patient struggling for life, and who will attempt to do everything possible to keep him cheerful and comfortable and to reassure him of early recovery Self feeding, washing and reaching out for objects should not be permitted The patient should receive assistance from the nurse Too many visitors should not be allowed so as to prevent any excitement or excessive talking In the very acute phase, no visitors should be allowed at all, except an occasional very close relative.

Rest of mind is just as important as rest of body. Hence, entrance of all business worries and family disturbances into the sick room is strictly to be prohibited Also, exciting radio programs or exciting stories read by the nurse should be strictly prohibited.

In many cases there is marked nervous irritability and extreme restlessness associated with the physical suffering and with the brain involvement due to congestion These cases should receive a sufficient amount of the opiates to keep them quiet and restful. Morphine sulphate $\frac{1}{8}$ to $\frac{1}{4}$ grain by hypodermic injection every four to six hours, if necessary, is most efficacious for that purpose. In those cases which show a marked sensitivity to the

drug, in the form of severe vomiting or retching, pantopon ⅓ grain or dilaudid $\frac{1}{16}$ grain may be tried instead An occasional case will respond better to one drug than the other Infrequently, any of these drugs may produce excessive depression of the respiratory center, shown by extreme slowing of respiration. This is more apt to occur in those cases which present Cheyne-Stokes respiration. In such cases the drug should be used very carefully and sparingly Should excessive respiratory depression occur, caffein sodiobenzoate 7½ grains or coramine, two to four cubic centimenters should be given intravenously or hypodermically, depending upon the urgency Coramine is preferable, if there is a great deal of irritability in spite of the narcosis If Cheyne-Strokes respiration is severe, a slow, intravenous injection of 7½ grains of aminophyllin is often efficacious Demerol 50 to 100 milligrams may be used to better advantage than the opiates in some cases

Dietotherapy Proper regulation of the patient's diet during the acute congestive phase and convalescence is an essential part of therapy This has been rightly stressed by Proger[32] He advises severe restriction of food intake at first and more moderate restriction over a period of two or three weeks during convalescence, with the loss of 10 per cent of the patient's weight

There are several therapeutic objectives in the dietary care of the patient First, we must supply the type of food that is easily digestible and assimilable and which prevents the distention of the gastro-intestinal tract Second, we must limit such food intake to a minimum so as to lessen the metabolic activities associated with the digestion and assimilation of food This results in slowing of the heart, lowering of the pressure, and a diminished cardiac output, all of which have the tendency to conserve the cardiac energy and help restore its function Third, we must avoid those products which tend to accelerate the heart or produce the arrhythmias, such as the excessive use of coffee or tea Fourth, we must reduce the amount of salt intake to a minimum to prevent the retention of body fluids

The usual routine advocated is to use the Karell diet, proposed in 1866 by a Russian physician This consists of 200 cc of milk given four times a day The total fluid intake is thus restricted to 800 cc., yielding 550 calories and only 1 6 grams of sodium chloride and 26 grams of protein per day The purpose of this diet is to restrict the fluid, salt and protein intake This fluid restriction, in addition to salt restriction is stressed in most textbooks

The author's personal experience has been that the limitation of fluid intake in congestive failure is not necessary In fact, an unrestricted amount of fluid intake is definitely advantageous, provided the salt intake is restricted The recent observations by Schemm[33] and by Burges and co-workers[34] appear to prove this assertion and should help eliminate the practice of strict fluid restriction.

A good routine in the acute congestive phase, is to allow the patient no other food than about five or six cups of fruit juices, sweetened to taste with pure glucose; either the syrup or the anhydrous form The juices are given in small amounts at frequent intervals Where the tendency to nausea and vomiting is present, it is best to dilute the juices with some water and serve cold *Enough water may be given in addition to bring the total fluid* intake to about two or three quarts a day Either orange, grapefruit, grape or prune juice may be used, depending upon the patient's likes and his reaction towards the particular juice In some cases a little of each may be used at different times to take away the monotony Inasmuch as the carbohydrate content of grape and prune juice is about double that of grapefruit or orange juice, it may not be necessary to add any glucose to the former

The carbohydrate content of grapefruit juice is about 20 grams per cup, orange juice 24 grams, grape juice 40 grams, and prune juice 46 grams The protein content of grapefruit and orange juice is about 2 grams per cup If we allow the equivalent of 180 to 190 grams of carbohydrates per day, made up of the above, the total intake will be about 750 to 800 calories per day The protein and salt contents in such a diet are negligible

As improvement progresses, we may add a cereal such as cream of wheat, and jello, junket, custard, cottage cheese, one egg, and vegetables It is advisable to watch the effect of some vegetables which have a tendency to produce flatulence, such as beans, peas, raw tomatoes, cabbage, cauliflower, broccoli, cucumbers, onions, garlic and the like All these should be avoided in individuals who can not tolerate them

The total caloric intake should be kept below 1,000 calories per day, well into convalescence *In children, however, the food intake should be* relatively greater and more proteins should be given

During late convalescence the food intake should be gradually increased and more solid food added In markedly obese individuals an 800 to 1,000 calory diet is to be continued for several weeks In the usual case an intake of about 1,000 to 1,200 calories per day in moderately fat individuals, and 1,500 to 1,800 calories in the person of average or less than average weight should be allowed The protein intake should not exceed 50 grams to keep the specific dynamic effects of the food to a minimum The bulk of the food, say about 250 grams per day, should be in the form of carbohydrates. If diabetes is present, enough insulin should be given to take care of the carbohydrate intake

The important fact we must bear in mind is to restrict the sodium chloride intake to a minimum, perhaps no more than one gram per day Well compensated cases may develop signs of congestive failure as soon as the amount of salt intake is increased to five grams per day or over, and if decompen-

sation is present an amount over two grams per day will interfere with recovery. This implies that no extra salt be added to food, and that all the foods be prepared without salt.

Inasmuch as it is the sodium radical of sodium chloride which is the responsible factor, no material containing sodium, such as sodium bicarbonate, sodium sulphate and others should be used. If palatability of food, due to lack of sodium chloride, is interfered with and deprives the patient of his appetite, some of the substitute salts obtained on the market may be used.

Digitalis Therapy: Digitalis produces its therapeutic effect in congestive heart failure in two ways. One is by slowing of the ventricular rate if auricular fibrillation is present, thus improving the cardiac function, as described in Chapter VII. The other is through its direct action on the myocardium. Slowing of the heart where the rhythm is regular does not always occur where the drug is given in therapeutic doses.

As was pointed out in the early part of this chapter, heart failure is due to diminished mechanical efficiency of the heart muscle There is excessive stretching with the transformation of the chemical energy into heat rather than mechanical work. Digitalis increases the mechanical efficiency of the heart muscle fibers. The muscle tone is improved, diminishing the excessive stretch of the fibers, and the force of muscular contraction is increased, resulting in a greater volume output.

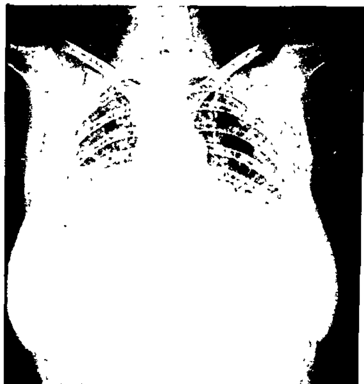
The form of digitalis to be used and the route of its administration in congestive failure varies with the urgency In acute, severe left heart failure with massive pulmonary edema, where there is great need for rapid digitalization, the intravenous route of administration is essential. Inasmuch as ouabain and strophanthin produce their full effect much faster than any other of the digitalis preparations these drugs are preferred. We must be sure, however, that no digitalis has been used for at least one week before. Ouabain is given intravenously in one dose of 0 25 to 0 5 mg Strophanthin K is given in one dose of 0 25 to 0 5 mg, slowly injected. It is always safer to give the smaller dose or less where there is any suspicion that the patient had received digitalis within two weeks. The full therapeutic effect of the drug is obtained within two hours Inasmuch as there is some individual variation in response to digitalis therapy, an additional amount may be required, when the smaller dose is used. This can be given by mouth in the form of digitoxin The amount depends upon the individual response.

The intravenous administration may also be used in congestive failure where the urgency is not very great, but where there is persistent vomiting due to gastro-intestinal or hepatic stasis. Here, the safer but more slowly acting preparations are to be used. Digitoxin 1.2 to 1.5 mg given intravenously in one dose produces its full therapeutic effects in four to six hours. It is safer, however, to give 0.6 mg. as the first dose, to be followed by smaller

doses given by mouth at four to six hour intervals until the full therapeutic effect is attained.

Where there is no urgency or vomiting, any of the digitalis preparations in the doses described in Chapter VII may be administered by mouth.

Whatever route of administration is used, the full therapeutic effect of the drug must be continued by giving a daily maintainance dose, as described in Chapter VII



radicals

In using digitalis in congestive failure without auricular fibrillation, it is at times difficult to decide if some of the symptoms the patient presents are due to overdigitalization or to the decompensation. It is most essential, therefore, to keep in mind the signs of digitalis toxicity. Some of these were mentioned in Chapter VII. More serious toxic manifestations such as sino-auricular standstill, auricular fibrillation, ventricular tachycardia,

and fibrillation are observed in occasional cases These disturbances, appearing after large amounts of digitalis have been used, call for immediate discontinuance of the drug, even though failure persists. In some cases where myocardial damage is extensive, toxic manifestations may develop before the full therapeutic effect of the drug occurs

The Use of Diuretics Many cases of congestive failure will recover under rest, careful dieting and digitalis therapy, as exemplified by the case repre-



FIG 73—SAME PATIENT AS IN FIG 70 Three weeks later on rest, diet and digitalis therapy

sented by Figures 72 and 73 Many others, however, are more obstinate and require the use of diuretic drugs for relief Still others, who present very acute distressing symptoms require the use of diuretics before the therapeutic effects of rest, diet and digitalization are tested

The mercurial diuretics are the most potent diuretics. The most effective and least toxic are salyrgantheophylline, mercupurin and mercuhydrine. The last has the advantage over the other two in producing less irritation and less pain when given intramuscularly All of these preparations contain theophylline besides mercury As marketed, salyrgan contains 39 6

mg. of mercury, mercupurin 39 3 mg., and mercuhydrine 39 mg. per 1 cc. of the solution.

The best route of administration is by intravenous injection Diuresis begins about two hours after such injection and the maximum response is reached in five to eight hours. The complete effect lasts about twenty to twenty-four hours, at the end of which time nearly all of the drug is eliminated. If given by the intramuscular route the effect of the drug begins a little later, but the duration of its action is about the same.

The intramuscular route is used where we cannot get into a vein, or where the diuretic effect of the intravenous route is too drastic or is associated with untoward reactions

Because the maximum effect of these diuretics occurs within five to eight hours after the injection, the best time for their administration is in the early morning hours. This will avoid disturbance of sleep during the night due to frequent desire to urinate

To avoid severe toxic reactions to the drug which an occasional patient may exhibit, it is advisable to give only 1 cc as a test dose. If no untoward effects occur within twenty-four hours, it may be repeated in 2 cc doses The frequency of repetition of the drug depends upon the severity of the cardiac decompensation and the diuretic response of the individual. Both of these may vary considerably in different patients The diuresis varies not only in different individuals with the same amount of failure, but also with the degree of failure and with the ability of the heart to respond to digitalis therapy. In some cases as much as 4,000 cc. of urine or more may be passed in twenty-four hours. Ramsden[15] reported an unusual excretion of as much as 14,500 cc in twenty-four hours.

In some cases the mercurials may be given rectally in the form of a suppository. The mercurin suppository may be used for that purpose It is advisable to precede its administration by a cleansing enema This method of administration is not to be used in the presence of colitis, proctitis, anal fissures or hemorrhoids and localized anal inflammation It is also inadvisable to use it if there is marked sensitivity to any local irritation, although in such cases coating the suppository with carbolated or even plain vaseline may, at times, overcome its irritating effect

Batterman and co-workers[16] recommend the oral administration of mercupurin, either in one dose of five tablets daily, or two tablets three times a day for two to four days. They found no evidence of kidney irritation and only mild gastro-intestinal irritation in some cases resulting from this method of administration. The best response is obtained when ammonium chloride and digitalis are given simultaneously. It is best adopted for those cases that do not require rapid removal of edema, or who can not tolerate an intravenous injection. The author has had insufficient experience with this

mode of administration of the drug He tried it in a few cases, but they all complained of gastro-intestinal upset following its use.

According to available experimental evidence, the diuretic effect of the mercurials is due mainly to their action on the kidneys, reducing the amount of tubular reabsorption. There is a possibility also, although not definitely proved, that these drugs have also some extrarenal effects in the elimination of the body fluids Thus, exudation of fluids from incision or puncture of the skin over edematous areas is much greater after the mercurials are given than before Also the loss of body weight is often greater than could be accounted for by the amount of urinary elimination when the mercurials are used, which suggests the possibility that elimination by the skin in the form of sweat may be promoted by these drugs

The diuretic effect of mercurials is often increased by the use of ammonium chloride This may be administered in the form of the enteric coated tablets, in doses of about thirty grains three times a day for two days before the mercurial is injected It is believed that the enhancing effect of the ammonium chloride is through the production of some degree of acidosis

The diuretic effect of the mercurials is interfered with, at times, by the presence of massive pleural effusion or ascites. Removal of these fluids by aspiration may be followed by improvement in their diuretic effect The opiates may, likewise, interfere with a proper diuretic effect of the mercurials in occasional cases

In some cases where the response to the ordinary doses is poor, double the dose given at one time may provide good results

The *untoward effects* of the mercurial diuretics may consist of mild fever, marked weakness, cramps in various muscles, thirst and general prostration These usually occur when the withdrawal of fluids is rapid and massive Excessive removal of fluids and sodium chloride by diuresis may in some cases be followed by cloudiness of mind, restlessness and delirium The administration of salt and fluid may soon overcome these symptoms.

More serious toxic reactions may occur Some of these may, in rare cases, be followed by death

Wexler and Ellis[37] classified the alarming toxic nonfatal reactions into immediate and delayed The immediate reactions may consist of "unpleasant" feeling, transitory dyspnea, apprehension, substernal discomfort, orthopnea and increase in the respiratory and pulse rate, moderate collapse, cyanosis, sweating with bradycardia or tachycardia The delayed reactions are asthmatic attacks and pulmonary edema In 2 of their fatal cases no significant pathology was found to account for death

DeGraff and Nadler[38] found 26 reported deaths in the literature up to 1942, in 16 years of the intravenous use of the drug Several more deaths have been reported since then The causes of death in 3 cases reported by

Volini and co-workers[39] were ventricular fibrillation in 2, and in the third, cardiac standstill Respiratory paralysis and asphyxia were causes mentioned by other authors.

Waife and Pratt[40] reported a fatal case following prolonged administration of mercuphylline. The postmortem findings consisted of nephrosis, hemorrhage in the ileum and colon and focal necrosis with hemorrhage of the liver. He quotes a similar case presented by Cabot

Severe toxic reactions usually occur in individuals who show untoward effects to an initial small test dose It is essential, therefore, to be extremely careful in such cases Inasmuch as no fatalities have, to the author's knowledge, been reported after the intramuscular injections, it is safer to use this method on any cases that show some disturbance after the initial test dose

Pines and co-workers[41] found experimentally that ventricular fibrillation in dogs caused by the mercurial diuretics could be prevented by the addition of 0 5 cc of 20 per cent magnesium sulphate to the mercurial solution They suggest its use in small amounts to prevent fatal accidents.

Chapman and Shaffer[42] found that ascorbic acid given prior to the administration of mercuhydrine reduced its toxicity No such effect was observed when used with the other mercurial diuretics

The xanthin and other diuretics Before the introduction of the mercurials, the xanthin group of drugs consisting of caffein, theobromine and theophylline and their derivatives, was used as diuretics In the order of their diuretic qualities, theophylline stands first, then theobromine and last caffein All these drugs have practically been abandoned in favor of the mercurials

Theophylline in 5 grain doses by mouth three times a day may, at times, result in considerable diuresis It should be given for only two or three days at a time with intervals of a week or more of rest, to prevent renal irritation which it often produces

Urea in doses of 15 to 30 grams three times a day, well diluted in water, given after meals, may at times produce a moderate diuresis It may be used in cases which can not tolerate the mercurial diuretics

Shaffer[43] obtained favorable diuretic effects from ascorbic acid given by mouth in doses of 500 milligrams daily. The effects were not as good when given intravenously. He also found that it enhanced the effect of mercupurin considerably.

The Use Of Oxygen. In cases of severe dyspnea, pulmonary edema, asthmatic or Cheyne-Stokes breathing as well as in the presence of marked cyanosis, oxygen therapy is very essential In extreme cases it may be life saving In all cases where oxygen is necessary it should be given continuously as long as needed. When not required it should not be used at all Its interrupted use is wasteful and has no effective value. For this reason also, the use of a funnel applied to the nose or mouth is practically valueless.

The best method of oxygen administration is by the *oxygen tent*, one type of which is shown in Figure 74. This method offers the additional advantage of lending itself to proper regulation of the temperature and humidity so as to keep the patient comfortable.

When the patient is first placed in the tent the flow of oxygen should be regulated to deliver 15 liters per minute. This is to be continued for about thirty minutes to bring up the concentration of oxygen within the tent to about 50 or 60 per cent. A similar flow should be used for about fifteen minutes every time the tent is opened for feeding or other purposes. The flow should then be continued at the rate of 8 to 10 liters per minute.

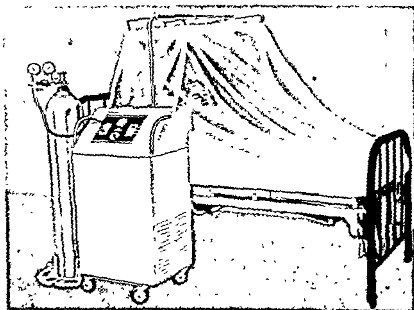


FIG 74.—OXYGEN TENT. There are several types and designs on the market. This one covers the entire body of the patient. Some cover only the upper part of the body.

This maintains an oxygen concentration within the tent of 40 to 60 per cent. The temperature in the tent should be maintained at 65 to 68° F and the humidity at 40 to 60 per cent. The oxygen concentration as well as the temperature and humidity should be tested from time to time.

The oxygen therapy should be continued as long as the patient exhibits the manifestations for which it is used. This may mean several days to weeks. Its discontinuance should not be abrupt, but by a gradual lowering of the oxygen concentration, first to 40 per cent for about one or two days, then to 30 per cent for one or two more days, and if there is no discomfort, it may then be discontinued.

Where pulmonary edema is very severe and is threatening life, we may use the positive pressure method of oxygen administration This is done by a *positive pressure mask.* The mask is equipped with a metal disk containing

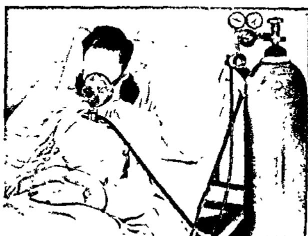


Fig 75—Positive Pressure Mask A small metal pillbox is attached to the facepiece which contains an expiratory valve with a movable calibrated disc By rotating the disc, we may obtain the desired centimeters of pressure

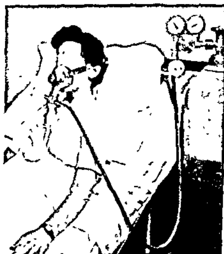


Fig. 76—Meter Mask A concentration meter having seven openings is attached to the tank, and the desired amount of admixture of air with the oxygen can then be regulated.

five orifices of varying diameters, as shown in Figure 75. The largest orifice offers no resistance The next four orifices offer resistances which result in an increase of positive pressure in the lungs, equivalent to 1, 2, 3 or 4 cm

of water corresponding to the amount of resistance offered by the given orifice. The positive pressure thus applied against the walls of the alveoli during expiration counteracts the tendency to capillary transudation. It also reduces the pulmonary vascular engorgement by compressing the vessels of the alveolar walls. The result is a rapid disappearance of the pulmonary edema and the relief from dyspnea

The positive pressure is increased gradually at fifteen minute intervals, one centimeter of water at a time up to a maximum of four centimeters, until signs of pulmonary edema disappear The pressure is then gradually lowered Automatic valves eliminate rebreathing

In some cases, we may use a meter mask by which we may regulate the flow of oxygen to as high a concentration as 100 per cent. This is accomp-



FIG 77—ONE OF THE METHODS OF THE APPLICATION OF OXYGEN BY THE NASAL ROUTE

lished by a special concentration meter attached to the source of oxygen, as shown in Figure 76 This concentration meter has several orifices of various sizes, any one of which may be kept open by adjustment, thus allowing a known amount of outside air to mix with the oxygen. In this way, the percentage of oxygen desired may be adjusted

The Boothby, Lovelace and Bulbulian mask, known as the B. L. B. mask is another form used for that purpose

For economy's sake and for convenience, it may be desirable at times to use a *nasal catheter* in the milder cases For this purpose a No. 10 French catheter is used Several perforations are made in its terminal inch, the catheter is lubricated and is passed through the nose down to the pharynx until its end reaches beyond the uvula The catheter is then fastened with adhesive to the forehead and nose and is connected with an oxygen tank An easier method for nasal inhalation of oxygen is shown in Figure 77.

A flow of 6 to 7 liters per minute by the nasal catheter reaching the pharynx will yield 40 to 50 per cent concentration of oxygen By the method shown in Figure 77, a concentration of 30 to 35 per cent may be obtained To prevent irritation of the upper respiratory passages, it is very essential that the oxygen passes through a humidifying apparatus.

For a more detailed description of oxygen therapy, the reader is referred to the monograph by Barach[44]

Possible Untoward Effects of Oxygen In the use of oxygen in cardiac therapy we must always bear in mind the fact that it may produce ill effects in certain cases where it is uncalled for and when given in very high concentration over a prolonged period Experimentally, many investigators have observed that prolonged breathing of high concentrations of oxygen in animals resulted in congestion and edema of the lungs, and if the exposure was further prolonged, death occasionally resulted

Comroe and co-workers[45] have tested the effects of continuous breathing of a concentrated atmosphere of oxygen for twenty-four hours in normal young males They found that a concentration of over 50 per cent produced substernal aching which was aggravated by deep inspiration, and signs of nose, throat and eye irritation as well as a marked decrease in the vital capacity The higher the concentration above 50 per cent the greater these disturbances were Stadie and co-workers[46] summarize a train of symptoms that may result from oxygen poisoning. Some of these are convulsions, syncope, loss of coordination, local muscular twitching, dizziness, unconsciousness, change in personality, slowing of mental ability and various other central nervous system disturbances. Respiratory disturbance may also occur

In the administration of oxygen it is essential, therefore, to use it only when *there are definite indications, and not to use a much higher concentration* than 50 per cent for a very long period

Management of Complicating Factors

There are many conditions that may be associated with heart failure which interfere with recovery Some of the more common are gastro-intestinal disturbances, general constitutional abnormalities, infections, venous thrombosis with pulmonary embolization and infarction, embolization to other parts of the body from mural thrombi in the heart, localized massive collections of fluids such as hydrothorax and ascites, and persistent, massive peripheral edema, which does not respond to the usual therapy The management of many of these complicating factors is discussed in later chapters, dealing with the respective conditions. Here we shall discuss, briefly, the management of the gastro-intestinal disturbances and of localized collections of fluids.

Gastro-Intestinal Disturbances These may consist of nausea, vomiting, constipation and abdominal distention

Nausea and vomiting may occur either as the result of marked congestion of the liver and the mucous membrane of the gastro-intestinal tract, or as a result of overdigitalization It is most essential, therefore, to decide definitely which is the cause in the given case When due to stasis, an increased amount of digitalis is called for to be given by a different route than by mouth When due to overdigitalization an immediate stoppage of the drug is necessary. In occasional cases the nausea and vomiting may be due to local irritation of the drug on the mucous membrane, as said before In such cases the symptoms are usually produced soon after the drug is taken, or before sufficient time has elapsed necessary for absorption

Nausea and vomiting may be considered to be due to stasis when the amount of digitalis given is not sufficient to produce toxic effects If auricular fibrillation is present, a ventricular rate of well over 100 beats per minute may mean insufficient digitalization In such cases the drug may be given in small doses intravenously or rectally every four to six hours until its full effect is produced Food should not be given by mouth if vomiting is severe Instead, glucose solution should be given slowly, intravenously either in the amount of 50 cc, of a 50 per cent solution two or three times during the day or 1,000 cc of a 10 per cent solution by a very slow continuous venoclysis, not more than at a rate of 15 drops per minute The concentrated solution is preferable where left heart failure is predominant The nausea and vomiting usually subside under such therapy within a day If not, it may be continued another day until the full effect of the digitalis is reached and gastro-intestinal stasis is reduced

Overdigitalization as a cause of nausea and vomiting is to be suspected when cardiac manifestations of digitalis intoxication are present, as described before and when the amount of digitalis given was in excess of that required. In this respect it is interesting and important to note that the pure glycosides, which have come into greater use of late, have been found to produce earlier and more severe toxic symptoms than the ordinary preparations of the whole leaf The author observed mild toxic effects in several cases, as said in Chapter VII, after full "digitalizing doses" were given. Flaxman[47] recently reported 30 cases of digitoxin poisoning in a short period of thirteen months and emphasized the fact that such poisoning is comparatively seldom seen when the whole leaf preparations are used He stresses the fact that considerable caution be exercised in the administration of digitoxin preparations in the advised dosage

Constipation, if present, may be relieved by small doses of magnesium sulphate, cascara or milk of magnesia No cathartic containing sodium should be used In some cases a soap suds enema may be required.

Abdominal distention is often relieved after a proper bowel movement. In some cases where the distention is marked and is not thus relieved, the use of a rectal tube or turpentine stupe may be of help.

Hydrothorax This, if marked, may interfere with proper therapy. Aspiration will not only relieve symptoms, but will also help improve the effects of rest, digitalis and diuretics. The author has observed several instances where aspiration of a massive hydrothorax was followed by effective response to the usual therapy of congestive failure where previously the response was very poor

In aspirating a pleural effusion, the necessary aseptic precautions should be employed and one or two cubic centimeters of 0.5 per cent novocain or procain be injected partly intradermally, and the rest in the deeper tissues. A needle two or three inches long is used, and care is to be taken to insert it in the selected intercostal space close to the upper margin of a rib rather than to the lower margin of the rib above, to prevent injury to the intercostal vessels and nerve Aspiration should be done slowly. If there is massive effusion a Potain suction bottle, or a similar device may be used, but not all the fluid should be withdrawn at one time If cough, pain, hemorrhage or a fainting sensation should occur, the aspiration should be stopped at once.

Ascites The milder grades of ascites are not infrequent in marked congestive failure and usually respond well to ordinary therapy. Severe grades of ascites are infrequent in congestive failure They are more common in constrictive pericarditis However, in occasional cases of long standing and advanced congestive failure, marked ascites may be present.

Severe ascites due to any cause, which does not respond to the usual therapy requires paracentesis or aspiration. This may safely be done at home. The procedure is as follows:

The bladder is to be fully emptied by voluntary urination, or, if necessary, by catheter. The patient should then be in a sitting position on a chair. The legs are separated and covered by a rubber sheet. A large bucket is placed near the chair, between his feet. The area selected for the insertion of the trocar should be in the midline of the abdomen at a point midway between umbilicus and the pubis Proper sterilization is important, and the local area is to be fully anesthetized by novocain injection, as for aspiration of the chest. A very small incision through the skin may be made which usually facilitates the insertion of the trocar. In some cases this is not necessary. The trocar is forced into the abdominal wall by gradual, rotary movements [illegible]

[illegible] as a result of plugging the cannula by omental tissue, the trocar should be temporarily reinserted to push away the obstruction.

After the aspiration, compression of the abdomen by an abdominal binder is advisable to prevent the possible occurence of shock due to sudden relief of the intra-abdominal pressure.

Uncontrollable Peripheral Edema: With our present day therapy of congestive failure, massive persistent peripheral edema is uncommon. It is, however, still observed in occasional cases Here, Southey's tubes may be used. These are small, hollow cannulas 5 centimeters long and 3 millimeters in diameter, having many small openings in their walls. They are inserted, with their trocars, into the subcutaneous tissues of the edematous areas, after anesthetizing the skin. The trocars are then removed and the exposed ends of the cannulae are connected with long sterile rubber tubes, which lead to a collecting basin or bottle under the bed.

In some cases we may drain off, by this method, as much as three to four quarts of fluid from the tissues in twenty-four hours Removal of subcutaneous fluid by this means occasionally improves the response to mercurial diuretics.

Management of Acute Paroxysmal Nocturnal Dyspnea and Pulmonary Edema

Attacks of acute paroxysmal nocturnal dyspnea call for energetic therapy to prevent the onset of pulmonary edema, and, at times, sudden death

To prevent attacks the patient must avoid a large evening meal, and no food should be taken for at least four hours before bedtime. When in bed he must be in a propped up position If the attacks tend to come on frequently, a suppository of aminophylline 7½ grains, and phenobarbital ½ grain inserted rectally before retiring may be of help Proper digitalis therapy and measures taken to prevent cardiac failure, described before, should be employed

If a sudden, severe attack develops the patient is to be put up in a sitting position, properly supported. Morphine sulphate ⅙ to ¼ of a grain together with atropin sulphate 1/150 to 1/100 of a grain should be given hypodermically at once An intravenous injection of 7½ grains of aminophylline in 50 cc of 50 per cent glucose solution, given very slowly may give quick relief The administration of oxygen under positive pressure, as described before, is often necessary

In the absence of the anginal syndrome, coronary thrombosis or hypertension, adrenalin hydrochloride 1:1000 solution may be given hypodermically in doses of 10 to 15 minims, if the asthmatic breathing is severe, and is not relieved by the above treatment. This drug, however, is risky, and should be used as a last resort. In cases of severe hypertension, nitroglycerine 1/100 grain, placed under the tongue, may bring relief.

If severe pulmonary edema develops in spite of this treatment, or if we first see the patient during such an attack, a phlebotomy, rapidly performed,

may occasionally be life saving This is true especially when peripheral venous stasis is evident. This may be done by inserting a large caliber needle in one of the antecubital veins, and withdrawing the blood by a syringe This method, however, is often too slow and clotting frequently prevents rapid aspiration The best method is to cut down on one of the large veins The flow is then very rapid

The amount of blood to be withdrawn depends upon the severity of the attack, the general condition of the patient and the response while the blood is drawn. Usually 500 cc is sufficient, although in some cases smaller amounts suffice, and in others as much as 1,000 cc has to be withdrawn before relief is obtained In undernourished, cachectic and anemic individuals, a phlebotomy should not be done

In some cases a so-called dry phlebotomy may be attempted Four tourniquets or blood pressure cuffs are applied to the upper parts of the four extremities and are sufficiently tightened to obstruct the venous return to the heart, but not obliterating the arterial pulse completely This may be continued for fifteen to twenty minutes, at the end of which time considerable improvement is usually noted

Proper digitalization and use of oxygen, as described before, are most essential in the therapy of acute pulmonary edema

REFERENCES

[1] Nomenclature and Criteria For Diagnosis Of Diseases Of The Heart New York Heart Association, New York, 1939

[2] Redfield, A C, and Medearis, D N · The content of lactic acid and the development of tension in cardiac muscle Am J Physiol 77:662, 1926

[3] Starling, E. H, and Visscher, M B The regulation of the energy output of the heart. J. Physiol 62 243, 1927.

[4] Suarez, J R E, Fasciolo, J C, and Taquini, A C Cardiac output in heart failure Am Heart J. 32 339, 1946.

[5] Macleod, J. J R Physiology and Biochemistry in Modern Medicine St Louis, C V Mosby Co, 1927. Page 558

[6] Luisada, A A, and Sarnoff, S J Paroxysmal pulmonary edema consequent to stimulation of cardiovascular receptors Effect of intra arterial and intravenous infusions Am. Heart J. 31:270, 1946

[7] Heyer, H. E. Abnormalities of the respiratory pattern in patients with cardiac dyspnea Am. Heart J. 32 457, 1946.

[8] Pratt, J. H. Cardiac asthma. J A.M.A 87 809, 1926

[9] Pembrey, M. S., and Allen, R W.· Observations upon Cheyne-Stokes respiration. J. Physiol. 32 1929

[10] Meakins, J.: Distribution of jaundice in circulatory failure J. Clin Investigation 4 135, 1927.

[11] Epstein, A. A : A contribution to the study of the chemistry of blood serum. J. Exper. Med. 16:719, 1912.

[12] Warren, J V, and Stead, E. A. Fluid dynamics in chronic congestive heart failure· An interpretation of the mechanisms producing the edema, increased plasma volume and

elevated venous pressure in certain patients with prolonged congestive failure. Arch. Int Med. 73 138, 1944.

[13] Merrill, A. J: Edema and decreased renal blood flow in patients with chronic congestive heart failure Evidence of "forward failure" as the primary cause of edema J. Clin. Investigation 25 389, 1946

[14] Reichsman, F., and Grant, H · Some observations on the pathogenesis of edema in cardiac failure. Am Heart J 32.438, 1946

[15] Landis, E M, Brown, E, Fanteux, M, and Wise, C.· Central venous pressure in relation to cardiac "competence," blood volume and exercise J Clin Investigation 25 237, 1946

[16] Fetterhoff, G, and Landis, H R M Compression of pulmonary veins the pressure factor in the etiology of cardiac hydrothorax Am J M Sc 138-712, 1909

[17] Dock, W The anatomical and hydrostatic basis of orthopnea and of right hydrothorax in cardiac failure Am Heart J 10 1047, 1935

[18] Drinker, C K Pulmonary Edema and Inflammation Cambridge, Harvard University Press, 1945

[19] Lundsgaard, C., and Van Slyke, D D Cyanosis. Medicine 2 1, 1923.

[20] Comroe, J. H, Jr, and Botelho, S · The unreliability of cyanosis in the recognition of arterial anoxemia Am J M Sc 214 1, 1947

[21] West, H F Clinical studies on the respiration A comparison of various standards for the normal vital capacity of the lungs Arch Int. Med 25 306, 1920

[22] Edwards, D J, and Wilson, M G An analysis of some of the factors of variability in the vital capacity measurements of children Arch Int Med 30 638, 1922

[23] Blumgart, H L The velocity of blood flow in health and disease Medicine 10 1, 1931

[24] Weiss, S, Robb, G P, and Blumgart, H L The velocity of blood flow in health and disease as measured by the effect of histamine on the minute vessels Am Heart J 4 664, 1929

[25] Winternitz, M, Deutsch, J, and Bruell, Z Eine klinisch brauchbare Bestimmungsmethode der Blutumlaufszeit mittels Deutsche Med Klin 27 986, 1931

[26] Robb, G P, and Weiss, S A method for the measurement of the velocity of the pulmonary and peripheral venous blood flow in man Am. Heart J 8 650, 1932-33.

[27] Fishberg, A M, Hitzig, W M, and King, F H Measurement of the circulation time with saccharin Proc Soc Exper Biol & Med 30 651, 1933

[28] Hitzig, Wm. The use of ether in measuring the circulation time from the antecubital veins to the pulmonary capillaries Am Heart J 10 1080, 1935

[29] Gross, D Measurement of the lung-to-face time by amyl nitrite Am Heart J 30 19, 1945

[30] Nathanson, M H, and Elek, S R The influence of heart size on the circulation time Am Heart J 33 464, 1947

[31] Williams, R H, and Rainey, J The causes of death in patients with congestive heart failure Am Heart J 15 385, 1938

[32] Proger, S Diet and heart disease, modern concept of cardiovascular disease Am Heart A 8 12, 1939

[33] Schemm, F R A high fluid intake in the management of edema, especially cardiac edema II Clinical observations and data Ann Int Med 21 937, 1945

[34] Bridges, W C, Wheeler, E O, and White, P D Low sodium diet and free fluid intake in the treatment of congestive heart failure New England J Med 234 573, 1946

[35] Ramsden, G F E Extreme response to a mercurial diuretic Brit M J 1 1159, 1936

[36] McCormack, J E, Batterman, R C, and DeGraff, A C The effectiveness and safety of mercupurin administered orally J A M.A 124 1243, 1944

[37] Wexler, J, and Ellis, L B · Toxic reactions to the intravenous injection of mercurial diuretics Am Heart J. 27 86, 1944

38 DeGraff, A. C., and Nadler, J E . A review of toxic manifestations of mercurial diuretics in man J.A M A. 119:1006, 1942.
39 Volini, I F , Levitt, R. O , and Martin, R.: Studies on mercurial diuresis V. Sudden death following intravenous injection J A M.A 128 12, 1945.
40 Waife, S O , and Pratt, P. T Fatal mercurial poisoning following prolonged administration of mercurophylline. Arch Int Med 78 42, 1946
41 Pines, I., Sanabria, A , and Arricus, R T. H Mercurial diuretics The addition of magnesium sulphate to prevent the toxic effects of their intravenous administration Brit Heart J 6 197, 1944.
42 Chapman, D W , and Shaffer, C F Mercurial diuretics A comparison of acute cardiac toxicity in animals and the effect of ascorbic acid on detoxification in their intravenous administration Arch. Int. Med 79 449, 1947.
43 Shaffer, C F The diuretic effect of ascorbic acid. Preliminary report on its use in cardiac decompensation J A M A 124 700, 1944.
44 Barach, A L Principles and Practice of Inhalational Therapy Philadelphia, J B Lippincott Co , 1944.
45 [illegible]
46 [illegible] 1944.
47 Flaxman, N Digitoxin poisoning. Report of 30 cases Am J M Sc. 216 179, 1948

CHAPTER XIV
Angina Pectoris

)RECORDIAL pain and other local chest disturbances, with or without radiation to other parts of the body, are the most frequent symptoms that ing the patient to the attention of the physician These disturbances cur in a certain characteristic manner in coronary insufficiency, but other seased states of the cardiovascular system, as well as extra-cardiac disse may exhibit them in some form or another.

Because of the great importance of a proper diagnosis of coronary insuf-:iency, which is commonly manifested by the anginal syndrome, we will ıalyze and fully describe this syndrome and differentiate it from similar anifestations occurring in other conditions

Definition: The term *angina pectoris* was first used by Heberden[1] in 1768 › describe a "disorder of the breast marked with strong and peculiar symp-›ms and sense of strangling and anxiety" In most of his cases, the ttacks came in "sudden fits" and he, therefore, attributed them to a "spas-ıodic, not inflammatory" condition The use of the term angina pectoris as continued to this day and should be preserved even if it does not fully escribe the condition It may best be defined as a symptom-complex haracterized by retrosternal or precordial pain, oppression, constriction r other sensations with characteristic radiation, brought about by strain, xcitement, exposure to cold and other factors and in occasional cases, ap-›arently spontaneously

Underlying Causes Angina pectoris is not a disease but a symptom, and n many cases a symptom-complex of a diseased state What the underly-ng disease might be has been a matter of speculation and much theoriza-:ion all through the years since Heberden first described the condition The present conception, well founded on experimental and clinical ob-servations, is that the main underlying cause is insufficiency of the coronary circulation, resulting in myocardial ischemia and anoxemia The degree of such insufficiency may be measured in most cases by the onset of angina pectoris under various grades of activity If the condition develops during extreme physical or mental strain, the degree of insufficiency may be considered to be slight If it develops under moderate strain, the degree is more marked. If, after the slightest exertion, it is very marked and if it comes on at rest, it is usually grave

We will limit our discussion of coronary insufficiency here to a physiologic

inadequacy of the coronary blood supply, leaving the subject of structural coronary occlusion for a later chapter.

Coronary insufficiency may be due to actual interference with the coronary flow to the myocardium or to relative inadequacy. Of the former, the most common pathologic condition is diffuse or localized coronary sclerosis, extending to the arteriolo-capillary portion of the coronary system. In the vast majority of cases of angina pectoris, coronary sclerosis is the underlying pathologic state. Keefer and Resnick,[2] in a review of the literature and in their own cases, found the presence of coronary sclerosis on autopsy in 381 of 399 cases who presented the anginal syndrome during life.

Rarer pathologic conditions causing angina pectoris are: syphilitic aortitis or other diseased states of the aorta affecting the coronary ostii, aortic insufficiency or marked aortic stenosis, especially the calcific type, infectious or rheumatic coronaritis, thromboangiitis obliterans of the coronary vessels or periarteritis nodosa.

A typical example of angina pectoris occurring in valvular disease is the case of a male, 27 years old. He had rheumatic fever at 9 years of age which debilitated him for over a year and resulted in chronic aortic and mitral insufficiency and low grade mitral stenosis. Under a relatively restricted life, avoiding too much exertion, he was asymptomatic till 26 years of age. At that age, with the assumption of greater responsibility of married life and as a successful architect, he began to experience left upper precordial pain on effort. This gradually became more pronounced so that at 27 years of age, the pain would appear rather frequently, in more severe form and often without any apparent provocation. Its location was mainly in the left upper precordium, radiating to the left side of the neck and down the left arm to the finger tips. He described his symptoms as "cramplike pain that takes all energy out of me." Each attack would last three to ten minutes and was immediately relieved by nitroglycerine.

Relative coronary insufficiency producing angina pectoris may occur in cardiac hypertrophy due to any cause. Here relative ischemia occurs as a result of hypertrophy of the individual muscle fibers, which becomes more marked under strain, as described in Chapter VI.

Coronary insufficiency resulting in angina pectoris may occur occasionally also in paroxysmal tachycardia, as shown by Barnes and Willius[3] and in hyperthyroidism, as shown by Sturgis.[4] In such cases, the increased cardiac activity and the shortened diastolic period result in a relative inadequacy of blood supply to the heart. Severe anemias may also produce angina pectoris, as shown by Herrick.[5]

The Provocative Causes. Although the fundamental basis of angina pectoris is insufficiency of the coronary blood supply to the heart and this insufficiency exhibits itself in the majority of cases on exertion, when the

heart muscle demands a greater blood supply than the coronary system can deliver, such insufficiency does not fully explain this phenomenon In the first place, a good many cases with severe enough coronary disease to produce congestive failure, may be free from angina pectoris while others with apparently low grade or no demonstrable coronary disease, as determined by clinical and electrocardiographic findings and as judged by the number of years some of these patients live, may exhibit the anginal syndrome in a more or less marked degree Furthermore, many anginal sufferers may be free from attacks for long periods of time or during certain hours of the day and have severe attacks at other times Evidently there are some additional factors which operate in bringing about an attack. Some of these are known, others are still not fully understood.

The most important factor is the presence of a sensitive nervous system which easily responds to nocuous stimulation It is a common observation by all physicians who have experience with cases of angina pectoris that the sufferer is usually a highly sensitive, emotional, excitable, erratic and nervous individual His nervous reactions to internal and external environmental changes are very marked and often exaggerated. With this background, we can understand how any extrinsic environmental disturbances or abnormal intrinsic bodily states will result in a marked reaction.

There is a multiplicity of disturbing environmental factors one meets in life The strain and stress of business or professional life, the hurry and bustle in the various occupational pursuits, the high tempo of our present civilization, in general, all have their irritating effect upon the nervous system This is particularly true in the highly sensitive and competitive individual These elements undoubtedly have a sensitizing influence upon the cerebral centers having to do with perception of pain and other symptoms of the anginal syndrome, thus preparing the ground for attacks

Besides the nervous factor induced by environmental conditions which may be provocative, there are other conditions that may act as trigger mechanisms, such as distention of the stomach by overeating, recurring exacerbation of chronic gall bladder disease, the use of tobacco, an excessive amount of coffee or tea, exposure to cold, loss of sleep and long fatiguing automobile trips

The effect of overeating in inducing attacks of angina pectoris in susceptible individuals is a common experience of all clinicians In fact, some sufferers from angina may develop attacks on exertion even after an ordinary meal, and will be free from symptoms following the same amount of exertion performed on an empty stomach

The effect of tobacco in inducing an attack is controversial The autho

angina-like attacks which stopped on the cessation of smoking. Bryant and Wood[6] observed a case of "pure tobacco angina" and in another where pain occurred on exertion, and tobacco, among 16 cases of angina pectoris. Moschcowitz[7] observed 4 cases with anginoid pain which stopped on the cessation of smoking. Several other authors have attributed to tobacco occasional cases presenting the anginal syndrome. Boyle and co-workers[8] observed no significant differences in response to intravenous injection of nicotine in normal individuals, in cases with coronary disease and in those with peripheral vascular disease. In 2 cases with spontaneous angina pectoris, however, pain occurred after the injection Pickering and Sanderson[9] feel that the term "tobacco angina" is not justifiable. They cite 3 cases where pain was induced or aggravated by smoking, but exercise tolerance was not reduced by it.

That tobacco smoke produces constriction of the peripheral blood vessels has been demonstrated by Wright and Moffat,[10] Lampson,[11] and various other observers. It seems, however, that such constricting effect on the coronary vessels does not occur frequently and in a sufficient degree to produce transient coronary insufficiency with the anginal syndrome. It is probable that the occasional occurrence of anginal pain on the use of tobacco is due to vago-sympathetic irritation induced by nicotine and the other products of tobacco smoke such as CO, methyl alcohol, aldehydes and so on The vago-sympathetic irritation may perhaps, also, account for the occurrence of some electrocardiographic changes induced by tobacco in some cases, as described elsewhere[12] It is very likely that tobacco does induce some coronary spasm, but not of sufficient degree to produce coronary insufficiency and pain in most cases

The effect of cold in inducing attacks has been definitely established We frequently see patients who are free from symptoms while in a warm room, but who develop an attack as soon as they are exposed to cold air Freedberg and co-workers[13] observed that application of ice to the hand reduced exercise tolerance in anginal cases. This effect was nullified by the application of heat or nitroglycerine.

A rare cause of angina pectoris is hypoglycemia, exemplified by the following case: A female, 47 years old, gave a history of recurring left precordial pain for a period of ten years, coming on mainly in the middle of the night or in the early morning hours, as well as on marked exertion The pain was usually associated with a fainting sensation, nervousness, pallor and extreme weakness, as if "the whole body is like a mass of lead" The heart was of normal size and shape, its rate was about 92 to 100, regular and the sounds were of good quality. The electrocardiogram was normal. The blood pressure was, systolic 132, diastolic 80. There were minimal sclerotic changes of some of the peripheral vessels and of the aorta.

The similarity of most of the symptoms to hypoglycemic shock and their occurrence mainly in the early morning hours made the author suspect a hypoglycemic state as the underlying cause. A fasting blood sugar obtained not during an attack, showed 66 milligrams per 100 cc of blood. A sugar tolerance test showed 131 milligrams after the first ½ hour, 139 after one hour, 80 after two hours and 78 after three hours. No attack occurred at the end of that period. Evidently, during attacks, the blood sugar level sank much lower. The symptoms, including the anginal pain were relieved by sugar taken by mouth in large amounts during the attack.

Another very rare condition that may apparently produce anginal attacks is a hyperactive carotid sinus reflex, two cases of which were reported by Friedman.[14]

Incidence of Occurrence: Angina pectoris is a very common condition, especially in the United States, and particularly in the large cities. Its incidence is much greater now than a generation ago. This will be apparent to one who has been in the practice of medicine for many years. It is possible that the condition progressively increases with the accelerated pace of our civilization.

The condition is more prevalent among males than females, but the incidence in the latter is rapidly increasing. This is probably due, mainly, to the fact that women are being attracted more and more to the occupational pursuits that were previously confined to men, as shown in recent statistics of the United States Department of Labor. It may, perhaps, also be due to a greater indulgence on the part of women in the use of tobacco.

It occurs most frequently after 50 years of age. Approximately 65 per cent of cases first come under observation after that age. It is, however, frequently observed, also between 40 and 50 years and we see many cases between 30 and 40 and even between 20 and 30. The author has observed instances in individuals younger than 20 and and even in childhood. With one exception, however, all had rheumatic cardiovalvular disease affecting mainly the aortic valve. The exception was a young man, 19 years old, who developed effort angina for three days, followed by an acute attack of coronary occlusion and electrocardiographic evidence of anterior wall infarction.

It appears that the incidence of the first appearance of the anginal syndrome is shifting towards the younger age groups in recent years.

Manifestations. Angina pectoris, like dyspnea in congestive failure, may be divided into two groups. In one, the attack is brought about by effort and in the other it occurs apparently spontaneously. The latter group is by far the more serious and usually occurs in individuals who suffered

from effort angina for a long time It is thus often a late manifestation of arteriosclerotic heart disease

Effort angina A typical case history of effort angina pectoris is the following: *An individual, usually past 40 years of age, who has enjoyed in* most cases perfectly good health before, finds after walking a distance of several blocks, especially up an incline, that he experiences an abnormal sensation in the upper sternal or midsternal region and in some cases in the lower sternal region, epigastrium or a little to the left towards the apex This abnormal sensation is described by some individuals as pain and by others as pressing, tightening, constricting, burning, cramping, choking, strangling, cutting or "heaviness" Occasionally the sensation is described by the patient as "gaseous pressure" or epigastric distress Some of the sensations, especially pain, may also be felt in various other areas in a radiating manner The most common is the left shoulder, the left arm, usually the inner portion, down to the elbow and in some cases as far as the wrists or even the fingers, usually the inner two In some cases, the pain or other sensation may radiate to both upper extremities, or only to the right Often they radiate to the back, in the interscapular region and occasionally to the neck, lower jaw, the ear, the mastoid, the throat or the upper abdomen As soon as he stops walking the pain or the abnormal sensation subsides

The character of the radiating sensation may at times be different than that felt over the precordium Thus in the precordium, there may be actual pain, while the sensation in the arms and hands may be described as "weakness," "heaviness," "numbness" or "tingling"

As time goes on, the patient finds that the attacks become more severe and appear after walking a shorter distance He must slow his pace of walking and he must stop for longer rest to get relief Nitroglycerine placed under the tongue gives earlier relief than rest alone and enables him to walk a longer distance without discomfort.

These recurrences may go on for weeks, months and in some cases for years before an acute episode of coronary occlusion supervenes or a sudden fatal attack occurs Usually, the more insidiously the symptoms develop the longer its course In cases where the symptoms are severe from their early onset, the condition is usually followed by an early attack of coronary occlusion. Thus, the author has observed many cases where the anginal syndrome developed on exertion in very severe form from the very first moment and in most of these, coronary occlusion occurred within one to three days after the onset of symptoms On the other hand, he has observed many cases where the anginal syndrome recurred in mild to moderate form many years before an acute episode ensued Some have died from other conditions than the heart disease

An interesting feature of effort angina is that different forms of exertion will bring about attacks in different individuals Thus, in a given case,

walking will produce an attack, whereas the patient may be able to do considerable manual work without discomfort. Another feature is that the same type of effort which usually brings about the anginal syndrome may, at times, fail to do so. It is very common to get a history showing that at times the patient is able to walk a considerable distance without discomfort and at other times he may not be able to walk more than one block before he develops an attack. Some of the factors that help provoke an attack in such cases are those mentioned under provocative causes. Of these, cold air, a heavy meal, nervous tension or excitement are outstanding.

Some cases will present the anginal syndrome in rather marked form in the city and be comparatively free of symptoms in the country. Some of these engage in considerable activity on their country estates with little or no discomfort but as soon as they come to the city, they begin to suffer symptoms. Evidently, the impurities in the air of the congested cities and the psychologic effect of the hurried life play their part in the production of symptoms in such cases.

The types of pain or other abnormalities experienced usually remain constant in the same individual. Its intensity, however, fluctuates to some extent during different attacks. The radiation, likewise, may occur at one time and not another in the same case. When it does occur, it always follows the same course in the given case.

In some cases, the pain or other abnormal sensations may first occur in the arms, the wrists or in the other areas and either remain localized there or radiate towards the chest. If it remains localized, it is often difficult to diagnose the condition. The author has in mind a patient who developed recurring severe attacks of pain in the left lower jaw. A dentist found a diseased tooth which he thought was the cause. Its removal, however, did not give any relief, in fact it aggravated the condition. A careful history revealed that the pain appeared mainly when climbing stairs or carrying a heavy object. Nitroglycerine gave immediate relief. At no time, did he have any similar pain in the precordium, but a sense of heaviness in that region did appear at times. He subsequently developed an attack of acute coronary occlusion.

In occasional cases, the anginal syndrome loses its identity entirely. The symptoms in such cases may be choking, marked precordial weakness, nausea or "gaseous pressure" in the epigastrium which may be relieved to some extent by belching. In such cases, the nature of the underlying disease is often hard to determine. In the more severe form, the condition may be associated with general body weakness, cold sweat, dizziness and fainting sensation.

Spontaneous angina pectoris. Some authors speak of this condition as "angina decubitus" because it often occurs when the patient is in bed. It

The attack usually comes on abruptly with great severity. There is a sense of severe precordial oppression, viselike constriction, choking sensation or severe pain with radiation as in severe effort angina. This is often associated with marked general constitutional reaction such as sweating, pallor, extreme tenseness, nervousness and fear of impending dissolution The blood pressure is usually elevated during the attack. The episode may be aborted in 2 or 3 minutes by nitroglycerine placed under the tongue. If not thus aborted, it may last 5 to 10 minutes and in some cases longer and then gradually subside In the vast majority of cases, nitroglycerine or even one of the opiate drugs must be used to give relief from the extreme suffering It may recur quite frequently and make life miserable

One who watches such an attack is struck with the marked nervousness associating it and which most likely precipitates it. The entire picture is suggestive of severe vaso-vagal disturbances associated with coronary angiospasm I have obtained electrocardiographic tracings in many such cases during the episode and after recovery from the attack and have found marked changes in the ventricular complexes during the attack, indicative of acute alterations in the myocardial state, corroborating the findings of other observers described elsewhere [12] This is one condition where the attack is evidently due to vaso-spasm of the coronary vessels causing acute coronary insufficiency. Anginal attacks occurring on excitement or emotional upset may also be classed under this heading although they cannot be considered spontaneous

Physiologic Mechanism· To understand the nature of angina pectoris it is essential to review briefly the physiologic mechanism of pain and associated manifestations

The perception of pain is accomplished by a special nerve center in the brain There is as yet no complete agreement as to the exact location of this center. It is believed to be in the lateral nuclei of the optic thalamus. Stimulation or irritation of the optic thalamus results in pain For proper perception, localization and finer discrimination of pain sensations an intact cerebral cortex is necessary, however. The center for pain here, as well as for touch, heat, cold and dimensional localization is situated in a sensory area localized in the anterior part of the superior parietal lobule and the angular giri According to Head and Holmes,[13] the cerebral cortex controls and checks the activities of the pain center in the thalamus

It is believed that afferent impulses for pain arising from different parts of the body such as the skin, the framework and visceral structures are not perceived by the same centers For the perception of visceral pain, the centers are probably located in various parts of the hypothalamic region which would explain the frequent association of vaso-vagal reactions with such pain.

The transmission of the pain impulses from their point of origin to the spinal cord and thence to the pain perceiving center is the same for the skin as for the body framework The impulses originating in the skin receptors travel along nerve fibers which make synaptic connections with fibers of the spino-thalamic tract in the posterior horn of the spinal cord. Each section of the surface of the body has its spinal segmental representation. Pain impulses from ligamentous, muscular and other framework structures of the body are also conveyed by somatic nerve fibers and make the same connections in the spinal cord. This pain, however, is not as sharply localized as that of the skin and is usually diffuse and is often felt at a distance. According to Lewis,[16] this is due to the fact that although the nerve fibers originating from the receptors in the various parts of the body framework also follow a segmental pattern, it belongs to a deep system and the structures where the receptors arise in most cases, extend beyond the given spinal segment where the nerve fibers enter.

Pain impulses from the various viscera are conveyed by afferent nerve fibers which run in the sympathetic nerve trunks through white rami communicantes to the posterior roots The synaptic connections and the course followed in the spinal cord is the same as for the sensory impulses arriving from the skin or from somatic structures The differences in the pain reaction to impulses originating in the viscera than those from other parts of the body are due mainly to difference in the number and arrangement of the sensory receptors in the viscera, the distance of these receptors from the segment of the cord where their fibers enter and their representation in the sensorium. Because the sensory receptors in the various viscera in the body are fewer in number and are at a distance from the given segments of the cord where their fibers enter, the pains arising from these structures are usually more vague and are felt at a distance from their actual seat of origin This is spoken of as *referred pain*. Such pain arising from a movable organ is often not easy to trace to its point of origin The heart being in a comparatively stationary position, however, sensory disturbances arising there are usually referred more or less correctly to its location.

Lewis disagrees with the hypothesis originally proposed by Sturgis that impulses from the viscera arriving in the cord diffuse from the gray matter representing the viscus to that representing the somatic structures of the same segment thus producing the referred pain. He believes that both are of central origin, the sensorium for the skin being represented in great detail, while that for the viscera in a massive and poorly defined fashion.

The painful impulses originating in the heart are carried by afferent fibers connected with the cardiac sympathetic nerves which course through the cervical and upper dorsal sympathetic ganglia and pass as rami communicantes of the upper five thoracic posterior nerve roots to the spinal cord. Thence,

they pass to the higher centers. Figure 78 illustrates diagrammatically the course of these nerves

The nature of the stimulus which produces cardiac pain, like other muscular pain, is at present believed to be a chemical or physico-chemical product resulting from muscular metabolism in the absence of a sufficient amount of oxygen

Kissin[17] had demonstrated that lack of oxygen in skeletal muscle during contraction brings about pain which continues even after the contractions

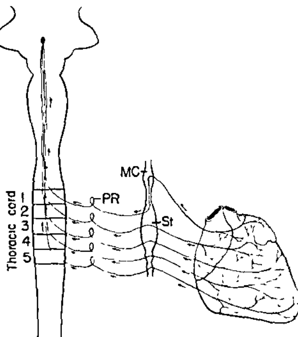


FIG 78—DIAGRAMMATIC REPRESENTATION OF THE COURSE OF THE AFFERENT NERVE FIBERS CONVEYING PAIN AND OTHER SENSORY DISTURBANCES FROM THE HEART TO THE CENTRAL NERVOUS SYSTEM MC, middle cervical ganglion, St, stellate ganglion, PR, posterior root ganglia Direction of flow of impulses indicated by arrows

have stopped, provided the local circulation is cut off The metabolites

muscle as well as to skeletal muscle

Rothschild and Kissin[18] produced the anginal syndrome by induced anoxemia and have also demonstrated some changes in the electrocardiogram in such conditions. Later, Levy and co-workers[19] have improved a method of producing anoxemia and employed the electrocardiographic

changes occurring under such conditions as an aid in the diagnosis of coronary insufficiency.

Spontaneous attacks of angina pectoris are undoubtedly caused by spasm of the coronary arteries which diminishes the blood supply to the heart muscle, as noted before The attack is therefore also due to the resulting myocardial ischemia rather than to the vascular spasm itself. The cause of sudden onset of such spasm is unknown An emotional upset may conceivably liberate adrenalin which may be the underlying cause in some cases.

The sensations of precordial tightness and choking are probably due to a viscero-motor reflex affecting the chest and adjoining muscles, similar to the abdominal muscular rigidity observed in acute abdominal disease

Hyperalgesia of the skin often observed over given areas is due, according to Lewis, to a nervous reflex passing through a special system of nocifensor nerves common to superficial and deep tissues This is a system of nerve axon connections within a given territory of cutaneous nerves The irritation of these nerves is a result of the products of injury

Conditions Simulating Angina Pectoris

There are various diseased states and nervous disturbances that may produce symptoms resembling those of angina pectoris The differential diagnosis in such cases is at times very difficult to establish This is especially true where the physical examination of the heart and other parts of the body show no abnormalities and the electrocardiogram is normal Even if abnormalities are found in the heart, the pain may not necessarily be caused by such abnormalities

The most important conditions that may produce angina-like symptoms are (1) disease of thoracic wall, (2) disease of the heart, other than ischemia, such as pericarditis, chronic valvular disease and so on, (3) an aortic aneurysm, (4) disease of the mediastinum, lungs and pleurae, (5) disease of the digestive system, (6) a diaphragmatic hernia, and (7) psychoneurotic disturbances

Disease of the Thoracic Wall Of the more common thoracic wall diseases that may at times produce confusing precordial pain and other abnormal sensations, the most important are intercostal neuralgia, pleurodynia, pectoral myalgia, herpes zoster and spinal arthritis

Intercostal neuralgia is characterized by pain occurring in spontaneous paroxysms, not strictly localized to the precordium and by the presence of tenderness in the involved intercostal spaces especially localized with maximum intensity at the 3 points of emergence of the branches of the intercostal nerves at the costo-sternal articulation, in the mid-axillary region and at the vertebral column.

Intercostal nerve pain due to pressure by fractured bones, by an aneurysm of the descending thoracic aorta and by new growths are usually of the girdle type, *not localized exactly to the precordium. The underlying cause* is often easily discoverable

Pleurodynia is a myositis involving the intercostal muscles. It is characterized by pain occurring during respiration and there is some tenderness along the course of the affected intercostal muscles

Pectoral myalgia is a painful condition of the pectoral muscles which may be caused by strain, trauma, fibrositis or myositis.

Strain and trauma of the pectoral muscles as a cause of precordial pain is occasionally observed in various industries. Mendlowitz[20] has observed instances of sprain of the pectoralis minor muscle in soldiers which produced pain in the precordial region simulating angina. The diagnostic feature of this condition is that the pain is reproduced by pushing the upper arm against resistance with the elbow in a position dorsal to the body.

Fibromyositis and myositis may be due to infections. The pain is localized to the pectoral regions and may be constant or may occur on movement of the arm. It may be dull or sharp, shooting or cramplike and tends to recur In fibromyositis, some nodulations are felt In suppurative myositis, the dense infiltrative pain and fluctuation make the diagnosis easy In nonsuppurative myositis, the condition usually involves various other *muscles of the body*

Herpes zoster is not difficult to diagnose after the herpatic eruption appears The author, however, has seen cases involving the left thoracic region, which were mistaken for angina before the eruption appeared If we bear in mind the fact that the pain here is not localized strictly to the precordium and is of root distribution, being very sharp, shooting with a marked hyperalgesia referred to the same region, the diagnosis cannot be mistaken even before the eruption

Spinal arthritis or spondylitis, the hypertrophic type, often occurs in association, with similar arthritis in various other parts of the body, but it may occur independently. It affects mostly the cervical and upper thoracic portions of the spine Infectious arthritis may occasionally affect the spine exclusively It may be recognized early by pain in the spine, not merely in the precordium; this pain is usually accentuated by bending the body Some spinal rigidity may be present. The condition should rarely give us any difficulty in differential diagnosis Roentgenologic studies of the spine are of help.

Disease of the Heart Other than Coronary Insufficiency: Precordial pain may occur in acute pericarditis and chronic valvular disease. The pain in such cases is usually *not as severe. The condition* will be discussed in later chapters.

Aortic Aneurysm· A large aneurysm of the ascending or the descending portions of the aorta boring its way to the surface of the chest may produce severe pain due to pressure and irritation of the intercostal nerves. The differential diagnosis in such cases is simple since the aneurysm can be easily discovered at this stage. The condition will be described in Chapter XXI

Disease of the Mediastinum, Lungs and Pleurae Angina-like pain due to acute and chronic inflammatory disease of these structures as well as to new growths is not difficult to differentiate from the anginal syndrome by physical and roentgenologic examinations. Acute episodes such as pulmonary embolization, spontaneous pneumothorax, sudden pulmonary atelectasis due to acute obstruction of a bronchus by a plug of mucus at the site of a new growth, spontaneous mediastinal emphysema, all may simulate an acute attack of coronary occlusion rather than of angina pectoris The differential diagnosis will be discussed in Chapter XX.

Disease of the Digestive System· Symptoms due to abnormalities or disease of the digestive system very often simulate those of the anginal syndrome Likewise, coronary insufficiency frequently exhibits itself in symptoms referable to the gastro-intestinal tract The reason probably is that the autonomic nervous system of the heart and the digestive system is connected by numerous intercommunicating nerve fibers. The referred pain and other sensations are thus confused and intermingled in consciousness

The most common abnormalities of the digestive system that may simulate the anginal syndrome are spasm, carcinoma or a diverticulum of the esophagus, organic and functional disease of the gastro-intestinal tract, dise[illegible] gall bladder and biliary ducts; and in rare cases, a diaphragma

[illegible] stuck dur- [illegible] of its passage. [illegible] often with [illegible] region [illegible] of the chest [illegible] which the patient is free from sy[illegible] he barium-filled esophagus, during the time when the [illegible] ill at once reveal the diagnosis. The spasm is usually located in the lower part of the esophagus

Carcinoma of the esophagus will also give the same symptoms as esophageal spasm early and can be recognized similarly. In the later stages, the condition cannot be mistaken.

A diverticulum of the esophagus is a much less common cause of angina-like symptoms. The diagnosis is made roentgenologically. An example is shown in Figures 79 and 80.

Organic disease of the stomach and intestines, such as gastritis, gastro-duodenal ulcers, carcinoma and others are usually characterized by symptoms of so-called "indigestion," consisting of a variety of sensations in the epigastrium or precordium or both The symptoms are described by the patient as burning, pressing, squeezing, fullness, distress and nausea The given sensation may radiate to the throat and there may be some regurgitation of fluid, giving the feeling of "heartburn" Often there is considerable belching



Fig 79—Diverticulum, D, of Upper Part of Esophagus, in a Male, 61 Years old In early phases, patient complained of recurring precordial pain and choking sensation, not related to exertion Later, the pain subsided but he developed slight dysphasia

due to swallowed air—aerophagea There may also be some intestinal distention and abdominal cramps, more or less constipation and the passage of mucus in the stools in the presence of mucous colitis.

The most distressing symptoms occur as a rule in duodenal ulcer, where the "heartburn" or pain develops about one or two hours after a meal and is relieved by food or alkalies

A rare condition that may produce severe attacks resembling angina pectoris or coronary occlusion is a diverticulum of the stomach. The author observed such a case in a female, 55 years old who was subject to severe

attacks of precordial pain radiating to the left shoulder, occurring in the middle of the night, while in bed. On sitting up or standing, the pain would disappear. Roentgenologic examination of the stomach, Figure 81, revealed a large diverticulum extending from the fundus which did not empty properly. Her heart, Figure 82, was normal.

According to Bloomfield[21] the various manifestations of gastro-intestinal disease are due to distention of the wall of the gastro-intestinal tube. He observes that the symptoms can be reproduced by introducing and inflating



FIG 80—SAME AS IN FIG 79 About fifteen minutes later, the diverticulum is

a balloon into the first portion of the duodenum He believes tl and spasm may easily occur in the complex muscular mechanism of the stomach and sphincters with potentialities for asynchronism.

From the character of the symptoms of gastro-intestinal disease if referred to the chest, we can see how difficult it may be at times to differentiate such disease from angina pectoris Furthermore, overeating and emotional upset may precipitate both conditions, as remarked by Harrison.[22]

Disease of the gall bladder may produce symptoms closely resembling the anginal syndrome Fitzhugh and Wolferth[23] have even observed significant

electrocardiographic changes in gall bladder disease which subsided after cholecystectomy. We have observed similar changes. In most cases, however, the differential diagnosis between the anginal syndrome and gall bladder pathology can be easily made.

An acute attack of cholecystitis usually has an abrupt onset with chills, fever, abdominal distress, pain and tenderness in the gall bladder region radiating to the right shoulder and scapula. Such an attack cannot be mistaken for cardiac disease Nevertheless, in occasional cases where the main



FIG 81—DIVERTICULUM, D, OF STOMACH, EXTENDING FROM THE FUNDUS, PRODUCING PRECORDIAL PAIN IN THE RECUMBENT POSTURE IN A FEMALE 55 YEARS OLD

symptoms are referable to the precordium, the condition may be mistaken for acute coronary occlusion

Diaphragmatic hernia This is almost always left-sided and may often give symptoms simulating angina pectoris The condition may be congenital or acquired, and is either in the nature of a perforating defect of all layers of the diaphragm or only of the muscular layer, the pleurae and peritoneum remaining intact. In some cases, there may be merely a relaxation of the diaphragm, either diffuse or circumscribed, a condition spoken of as eventration.

The symptoms may vary from digestive disturbances to severe vomiting,

dysphagia and chest pain radiating to the shoulder. If the protrusion is very large, there may be dyspnea, cyanosis, cough and severe chest pain We occasionally find some cases with extensive diaphragmatic hernias, however, without any symptoms. They may be discovered accidentally by

the day, and its compression of the lung. A pathognomonic auscultatory sign in extensive herniation is the presence of borborygmi.



FIG 82—SAME PATIENT AS IN FIG 81 Heart is within normal limits Aorta shows some knobbing Clinically or electrocardiographically, there was no demonstrable cardiac disease

A more frequent form of hernia simulating angina pectoris is that of the esophageal hiatus type. An example is shown in Figure 83. Nuzum[24] in a study of 100 cases, where the diagnosis of angina pectoris was made, found 25 who had evidence of an esophageal hiatus hernia In 22, the hernia was very small and in 3, large. He also observed that of 957 patients where the condition was looked for by x-ray, 12 per cent presented such herniation. The highest incidence in any other control group was only 3 per cent

Psychoneurosis and Neurocirculatory Disturbances: Such disturbances frequently present symptoms simulating closely the anginal syndrome. In many of these cases, the differential diagnosis is extremely difficult. It

must be remembered that the usual case of angina pectoris is nervous and irritable and it is therefore important not to regard any nervous individual complaining of symptoms closely simulating the anginal syndrome as a neurotic until every method of diagnosis has been used to rule out the presence of coronary insufficiency. In some cases, prolonged observation is necessary to establish a diagnosis. The subject of neurogenic heart disease will be dealt with in a later chapter.

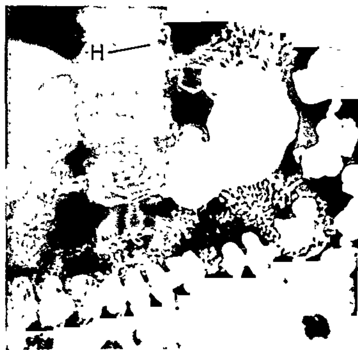


Fig 83.—Esophageal Hiatus Hernia, H, with Severe Recurring Precordial Pain for Two Years, not Related to Exertion. Pain relieved for two months following operation, and then the anginal syndrome set in. Male 52 years old.

The Diagnosis of Angina Pectoris

The most important means in establishing a diagnosis of angina pectoris is a careful history, for in about one-third of the cases, the physical, roentgenologic, electrocardiographic or other means of investigation may show nothing abnormal.

The history should include a careful inquiry as to the types of pain or other sensations felt, their location, radiation, intensity and circumstances under which the symptoms develop. A case is to be considered one of angina pectoris if the pain or other sensations, described in the earlier part of

this chapter, occur *on exertion, excitement or mental strain*. If the symptoms occur spontaneously and at no time do they appear on exertion or excitement, the condition is not to be considered one of angina pectoris unless the physical and other findings definitely indicate the presence of myocardial damage In such cases, the underlying cause of an attack may be distention of the stomach or other gastro-intestinal disturbances which produce coronary insufficiency reflexly. In some cases, the precordial pain may also be due perhaps to irritation or actual alterations of the nerve endings in the heart by the pathologic changes in the heart muscle Persistent or recurring spontaneous pain of this kind is often observed long after complete organization of an infarcted area, following coronary occlusion.

Severe recurring spontaneous attacks of angina pectoris are nearly always associated with arteriosclerosis and the examination in most cases reveals evidence of myocardial damage. All these cases usually also present the anginal syndrome on any physical or mental strain or excitement

Some of the abnormal physical findings that may help to corroborate the diagnosis are cardiac enlargement, abnormalities in the heart sounds, gallop rhythm, murmurs, hypertension and the presence of arteriosclerosis, especially involving the aorta. Roentgenologic examination is often necessary to demonstrate the presence of slight cardiac enlargement and early aortic sclerosis.

Electrocardiographic findings, described elsewhere,[12] may also help in arriving at a diagnosis. It must be understood, however, that neither the physical nor the electrocardiographic findings are specific of the disease.

In the author's experience, an important aid in the diagnosis of the anginal syndrome due to coronary sclerosis is the presence of a hyperactive cardioinhibitory carotid sinus reflex In a study of many hundreds of cases, he [25] found that this reflex occurs with greatest frequency and in highest degree in individuals with arteriosclerotic heart disease and has advocated its use as a diagnostic means in such a condition Nathanson[26] corroborated this finding

The test is very simple. With the patient sitting, the head is extended and pressure is applied to the carotid artery in the region of its bifurcation, at the level of the cricoid cartilage A positive response is exhibited by a marked slowing or stoppage of the heart. It is important to exert the pressure slowly and to one side of the neck at a time, for occasionally, marked dizziness, fainting, convulsions and other subjective disturbances may occur if too much pressure is exerted at once, as described elsewhere.[27]

Another test employed in doubtful cases is to breathe air containing a low concentration of oxygen for 10 to 20 minutes as described by Rothchild and Kissin[13] and Levy and co-workers.[13] In many cases of angina this procedure will produce the anginal syndrome as well as some abnormalities in the

electrocardiogram Similar results are often obtained by making the patient exercise

Adrenalin by injection may produce the same results but it is a dangerous drug to be used in suspected cases of coronary disease

We must always bear in mind the fact that angina pectoris due to coronary insufficiency may coexist with precordial pain due to one or more of the other conditions described above. In fact, the anginal syndrome may be accentuated by the coexistence of any one of the other conditions. It is important, therefore, to search for all possible causes of chest pain.

The differential diagnosis between agnina pectoris and coronary occlusion will be discussed in a later chapter

Prognosis of Angina Pectoris

Angina pectoris takes a very variable course Some individuals may go on for many years and may carry on considerable activity with fair comfort. Others, succumb to an acute attack of coronary occlusion or to some other cardiac accident, perhaps ventricular fibrillation or cardiac asystole, early in the disease.

In a study of 500 cases of angina pectoris by White and Bland,[28] the average longevity in 213 cases was 4.4 years after the onset of the disease. The average longevity for the entire series to the time of the report was 4.9 years. In 166 cases reported by Wedd and Smith,[29] the average longevity was 5 8 years About 15 7 per cent of cases lived 10 years or longer and 70 per cent of cases exceeded the calculated life expectancy.

In a series of 435 cases that I followed from the beginning of the disease to death, the average duration of life was 5 1 years There were 5 cases who lived 17 to 22 years, 14 cases, 11 to 15 years, and 21 cases, 7 to 10 years On the other hand, 85 died within one year and 60 of these within one-half year

Some of the factors that influence the longevity are the degree of coronary disease and myocardial damage, the sensitivity of the individual and the willingness on the part of the patient to live the restricted life necessitated by this disease

Cases associated with marked coronary sclerosis and myocardial damage, in whom the anginal syndrome occurs spontaneously, usually die very early in the disease They often have in addition to the anginal syndrome, repeated occlusions of the smaller branches of the coronary tree which precipitate attacks Also, individuals who are phlegmatic or insensitive to pain may succumb to attacks of angina pectoris early, for they usually develop the attacks late in the course of coronary disease. On the other hand, a sensitive individual may present the anginal syndrome when the amount of coronary insufficiency is comparatively insignificant.

Probably one of the most important factors that determines the longevity in angina pectoris is the willingness on the part of the patient to live a quiet and restricted life This is more obtainable in sensitive individuals who suffer symptoms on comparatively little exertion or excitement They learn early not to overstep the limits of their capacity for activity in order to avoid suffering. The insensitive as well as the careless type will either not have sufficient warning symptoms or will be unwilling to pay attention to proper advice. He will carry on his activities and his erratic life with disregard to any discomfort he may experience and will sooner or later suffer a crippling attack of a major coronary occlusion or die suddenly

The mode of death in angina pectoris varies. A great many, perhaps a third of the cases, die suddenly Many others develop coronary occlusion which may end in death. Some succumb to congestive failure and others to noncardiac complications

Treatment

General Care The most important therapy in angina pectoris is the avoidance of the type and degree of effort or excitement which bring about the slightest discomfort In mild cases this may merely mean the avoidance of unusual physical strain or mental excitation In very severe cases it may mean the entire elimination of all work and mental activity Between these extremes various degrees of restrictions are called for, depending upon the severity of the condition The criteria used in the determination of the amount of restriction are the same as in heart failure, described in Chapter XIII.

If drastic changes in the mode of living and activity are necessary in a given case, the advice to that effect should be given very tactfully, without alarming the patient or instilling too much fear in him It should be explained, to him, that it is not done because of the seriousness of his condition, but to prevent further damage

Inasmuch as knowledge on the part of the patient, that he harbors a serious heart disease may in itself act as a trigger mechanism for the onset of attacks, it is important that the physician minimize to the patient, the seriousness of the disease It is wise to tell the patient that every person of his age has some degree of thickening of the blood vessels supplying blood to the heart, but some individuals are more sensitive than others in perceiving the insufficiency of the blood supply resulting from the thickened vessels It is also wise to cite instances where people with such conditions lived on for many years All that is necessary is to exercise ordinary, sensible care As a person grows older he simply can not carry on the same activities as a young person The term "angina pectoris" is best not to be mentioned, for in the layman's mind, it is often synonymous with ex-

treme suffering and early death. When a patient is told elsewhere that he has angina pectoris, it is best to explain to him that this term has no specific meaning, and does not explain the exact nature of his particular condition

The general care to be employed in cases of angina pectoris is the same as in heart failure, described in the previous chapter

Inasmuch as certain factors act as "trigger mechanisms" in precipitating anginal attacks it is essential to remove, if possible, all such factors Overeating, excessive indulgence in alcoholic beverages, especially beer, exposure to cold air, indulging in exciting card games, horse races and other similar excitements must be prohibited in those individuals who experience attacks under such circumstances Certain intrinsic bodily diseases which help precipitate attacks such as biliary tract affections, thyrotoxicosis, anemia, active peptic ulcers and hypoglycemia should receive appropriate therapy Reduction of weight in the obese is essential The bowels should be regulated Foods which produce gaseous eructation and gastro-intestinal upset should be strictly avoided

Inasmuch as many sufferers from angina pectoris get severe attacks mainly in cold, inclement weather, it is advisable that the patient spend the winter months in a southern climate, when possible

If the attacks become very severe and recur frequently, a period of complete bed rest for two to six weeks is advisable for relief and to forestall, if possible, an attack of coronary occlusion which may be impending

Drug Therapy This is of no permanent value in this disease Aminophylline $1\frac{1}{2}$ to $4\frac{1}{2}$ grains or theobromine sodium or calcium salicylate $7\frac{1}{2}$ to 15 grains given three times a day by mouth have never definitely been proved to be of any value in this condition This also applies to other xanthine preparations marketed under attractive names The various conflicting reports in the literature of the value of these drugs by men whose reliability can not be questioned attest to the inconclusiveness of their decisions as to the beneficial effects of these drugs My personal experience is that if these drugs have any value in an occasional case, the disturbing side effects they often produce such as gastro-intestinal upset, headache, dizziness, lightheadedness and weakness counterbalance such value A critical analysis, however, leaves definite doubt if they have any value at all There are so many variable conditions that enter into the relief of symptoms in these cases that the effect of drugs can not be judged For instance, an increase in the amount of rest and sleep, improvement in weather conditions, better care of the bowels and eating habits, and improvement of domestic and business conditions are all factors favoring amelioration of symptoms Also, the psychologic effect of the use of a

given medication plays no small part in the relief of symptoms Finally, spontaneous fluctuation of symptoms must be considered in the evaluation of any therapy we employ

My personal observations are that a placebo produces the same effect in angina pectoris as any of the xanthin drugs This conforms with the observations of Gold and co-workers [38]

Nitroglycerine is one drug that has a definite effect in angina pectoris Its pain relieving effects, however, are short-lived, and the drug must be frequently repeated if attacks are recurring In some cases where an attack is expected to occur under an attempted strain, the drug may be given just before the strain is undertaken in order to prevent the attack from occurring

Nitroglycerine may be prescribed *in* $\frac{1}{200}$, $\frac{1}{150}$ *or* $\frac{1}{100}$ *grain tablet* The hypodermic rather than the triturate tablet should be used It is more soluble and more easily absorbable It should be given sublingually or chewed Its effect occurs within two or three minutes. In mild attacks the $\frac{1}{200}$ grain tablet is sufficient to give relief Where the attacks are severe the larger doses should be used.

The drug may be used as often as necessary and the patient must be assured that it is not habit forming, and that its use may be continued for many years without ill effects In occasional cases the side effects such as headaches, fullness in the head, flushing and palpitation may be disturbing These disturbances are minimized when smaller doses are used

When prescribing nitroglycerine it is very essential to specify that the tablet should be fresh The drug loses a considerable degree of its potency after standing on the druggist's shelf for several months It is also advisable, for the same reason, that no greater supply be prescribed for any patient at one time than he will require over a period of three months, or less Inasmuch as warmth deteriorates the potency of the drug, it should be kept in a cool place If the patient carries a bottle of tablets with him, as he should, it must be kept in an outside pocket so as not to come in contact with the warmth of the body

The sedatives, especially phenobarbital and bromides, are often of great value in relieving the tension and nervous excitation which often bring about attacks They also diminish the sensitivity and thus decrease the perception of pain These drugs are to be used only during periods when for various reasons there is a temporary increase in symptoms They should not be used for any prolonged periods

Nerve Block Paravertebral alcohol block may be used in intractable cases, that can not be relieved by the routine outlined above, and where the pain is very severe and repeatedly recurring This procedure is fairly

safe, if carried out by one who is thoroughly familiar with the anatomy and the methods of injection. A full description is to be found in the monograph by Mandl.[31]

REFERENCES

[1] Heberden, W Some account of a disorder of the breast Med Tr, Royal Col Physicians 2 59 1786

[2] Keefer, C S, and Resnick, Wm H Angina pectoris A syndrome caused by anoxemia of the myocardium Arch. Int Med 41 769, 1928

[3] Barnes, A R, and Willius, F. A Cardiac pain in paroxysmal tachycardia Am Heart J 2 490, 1927

[4] Sturgis, C C Angina pectoris as a complication in myxedema and exophthalmic goiter Boston M & S J 195 351, 1927

[5] Herrick, J B On the combination of angina pectoris and severe anemia Am Heart J 2 351, 1927

[6] Bryant, J M, and Wood, J E, Jr Tobacco angina An electrocardiographic study Am Heart J 34 20, 1947

[7] Moschcowitz, Eli Tobacco angina pectoris J.A.M.A 90 733, 1928

[8] Boyle, M N, Wegria, R, Cathcart, R T, Nickerson, J L, and Levy, R L Effects of intravenous injection of nicotine on the circulation Am Heart J 34 65, 1947

[9] Pickering, G W, and Sanderson, P. H Angina pectoris and tobacco Clin Sc 5 275, 1945

[10] Wright, I S, and Moffat, D The effects of tobacco on the peripheral vascular system J A M A 103 318, 1934

[11] Lampson, R S A quantitative study of the vasoconstriction induced by smoking J A M A 104 1963, 1935

[12] Sigler, L H The Electrocardiogram Its Interpretation and Clinical Application New York, Grune & Stratton, 1944 Pages 276–281, 366

[13] Freedberg, A S, Spiegle, E D, and Riseman, J E F Effect of external heat and cold on patients with angina pectoris, Evidence of the existence of a reflex factor Am Heart J 27 611, 1944

[14] Friedman, M The anginal syndrome as a manifestation of hyperactivity of the carotid sinus Am Heart J 29 37, 1945

[15] Head, H, and Holmes, G Sensory disturbances from cerebral lesions Brain 34 102, 1911–12

[16] Lewis, T Pain New York, The Macmillan Co, 1942

[17] Kissin, M The production of pain in exercising skeletal muscle during induced anoxemia. J Clin Investigation 13 37, 1934

[18] Rothschild, M A, and Kissin, M Production of the anginal syndrome by induced general anoxemia Am Heart J 8 729, 1933

[19] Levy, R L, Bruenn, H G, and Russell, N G, Jr The use of electrocardiographic changes caused by induced anoxemia as a test for coronary insufficiency Am J M Sc 197 241, 1939

[20] Mendlowitz, M Strain of the pectoralis minor muscle, an important cause of precordial pain in soldiers Am Heart J 30 123, 1945

[21] Bloomfield, A L Diseases of the digestive tract Musser's Internal Medicine, Philadelphia, Lea & Febiger, 1932.

[22] Harrison, T R Clinical aspects of pain in the chest II Pain arising from the esophagus Am. J. M Sc 209 765, 1945

[23] Fitzhugh, T, and Wolferth, C C. Cardiac improvement following gall bladder surgery,

electrocardiographic evidence in cases with associated myocardial disease Ann Surgery 101 478, 1935

[24] Nuzum, F R Hernia of esophageal hiatus: Its relationship to angina pectoris Am Heart J 33 724, 1947

[25] Sigler, L. H Hyperactive cardioinhibitory carotid sinus reflex a possible aid in the diagnosis of coronary disease Arch Int Med 67 177, 1941; The hyperactive cardioinhibitory carotid sinus reflex as an aid in the diagnosis of coronary disease, its value compared with that of the electrocardiogram New England J Med 226 46, 1942

[26] Nathanson, M H Rhythmic properties of the human heart Arch Int Med 72 613, 1943

[27] Sigler, L. H Subjective manifestations of the hyperactive carotid sinus reflex Ann Int Med 29 687, 1948

[28] White, P D, and Bland, E F A further report on the prognosis of angina pectoris and of coronary thrombosis A study of five hundred cases of the former condition and of two hundred of the latter Am Heart J 7 1, 1931

[29] Wedd, H M, and Smith, R E Observations on prognosis in angina pectoris Am J M Sc 189 690, 1935

[30] Gold, H, Kwit, N T, and Otto, H The xanthines (theobromine and aminophylline) in the treatment of cardiac pain J.A M A 108 2173, 1937

[31] Mandl, F (Translated by Kollner, G) Paravertebral Block New York, Grune & Stratton, 1947

CHAPTER XV

Paroxysmal Cerebral Ischemia. "Adams-Stokes Syndrome"

It was shown in Chapter XIII that congestive heart failure often produces serious mental disturbances. These are mainly due to a greater or less degree of anoxemia and cerebral edema.

In this chapter we shall describe the symptom complex resulting purely from intermittent cerebral ischemia. In the majority of these cases the underlying causes of the cerebral ischemia are disturbances in the cardiac mechanism, described in Chapter VII. In occasional cases the causes may be vasovagal abnormalities or a hyperactive carotid sinus *reflex*.

The Symptom Complex

The symptoms of paroxysmal cerebral ischemia vary with the duration of the acute ischemia and with the state of the blood supply to the brain before the acute paroxysm. Individuals with cerebral arteriosclerosis will develop such symptoms much more quickly, and the episode will last longer than those in whom the cerebral vessels are normal.

If the acute ischemia lasts only one to five seconds, there may merely be some confusion of thought, inability to concentrate on questions asked, dullness of mind, dizziness and darkness or fogginess before the eyes. In some cases, the causative factor is frequently repeated and the patient presents almost a continually dull state of mind. He may be oblivious to his environment, with confusion of thought, interspersed by short periods of clarity of mind. During these short periods, he usually does not remember what had occurred. Some of these episodes of transient ischemia may be associated with faintness and general weakness.

If an acute episode lasts ten to thirty seconds, faintness and dizziness is soon followed by coma and convulsions. Occasionally, local clonic convulsive movements of some parts of the body may occur before general convulsions develop. Preceding the onset of coma, some patients are aware that they are losing consciousness and attempt to sit down or grasp at some object to keep from falling. Others fall and suffer injury, evidently before they have a chance to protect themselves. During the comatose state, there is, at first, marked pallor of the face and later, cyanosis. When the attack is over, the face usually becomes red.

During a protracted attack lasting more than thirty seconds, the veins in the neck swell, cyanosis of the face may become marked, and severe,

generalized tonic and clonic convulsions occur, affecting all the muscles of the body There may be foaming from the mouth, involuntary passage of urine and feces and Cheyne-Stokes breathing may develop

The outcome of an attack varies with its duration and the previous state of the cerebral circulation. In rare cases, recovery may occur after an attack lasting as long as five or six minutes Most cases, however, succumb to attacks which last more than three minutes and some even to shorter attacks In experimental work on blood letting in dogs, Negovski[4] found that animals cannot be revived if clinical death, that is, if cessation of the heart beat and respiration, lasts longer than five or six minutes.

Recovery from a severe attack usually leaves the patient in a stuporous and drowsy state with marked confusion of thought for some time He does not remember what has occurred even after his mind becomes clearer

Mechanism

The symptoms that we recognize now as being due to paroxysmal cerebral ischemia, were first mentioned by Morgagni[1] in 1765 and were more fully described by Adams[2] in 1827 and particularly by Stokes[3] in 1846 The latter two authors noticed the relationship between the cerebral manifestations and cardiac disease, and both stressed the association of a slow pulse and the cerebral symptoms The symptom-complex of the cerebral disturbances together with a slow pulse, now understood to be due to heart block, has, *therefore, since been known as the "Adams-Stokes syndrome"* In view of the meager knowledge of physiology and pathology in their day, the underlying mechanism was not fully understood Adams found some distention of the vessels of the brain in his autopsy cases, and thought that congestion of the brain was the cause of the cerebral symptoms He argued that the distention might have been due to incapacity of the ventricles to empty themselves with sufficient quickness. Stokes clearly described the cardiac manifestations, which are now understood to be those of auriculo-ventricular block, although he did not, of course, know the *exact mechanism of the condition*

We shall confine our discussion mainly to the cardiac cause of paroxysmal cerebral ischemia, since it is here that the term "Adams-Stokes syndrome" may truly be used We shall also briefly discuss some of the vasovagal disturbances as well as the hyperactive carotid sinus reflex, which may induce the same syndrome Here, also, the condition is due mainly to disturbances in the cardiac mechanism, although other factors are operative in some cases

Paroxysmal Cerebral Ischemia due to Cardiac Disturbances

In this group may be included auriculo-ventricular heart block, transient ventricular fibrillation, and sino-auricular standstill. Milder grades of

transient cerebral ischemia may occasionally be observed, also, during a sudden onset of paroxysmal tachycardia, auricular flutter and auricular fibrillation, when the ventricular rate is extremely rapid

Judging from the description of the heart findings by Adams and Stokes, the term "Adams-Stokes syndrome" is applicable only to that caused by auriculo-ventricular heart block

Complete Auriculo-Ventricular Block This condition will result in symptomatic cerebral ischemia when sudden *ventricular asystole* occurs, lasting a variable period of seconds to minutes The severity of cerebral disturbances varies with the length of ventricular asystole, If longer than three to six minutes, death may ensue

In the majority of cases of complete auriculo-ventricular heart block with a variable duration of ventricular asystole, the condition is preceded for some time by the lower grades of block and can thus be recognized In rare cases, complete auriculo-ventricular block with ventricular asystole may develop suddenly without any previous conduction disturbances. The diagnosis in such cases can only be made during the attack when no heart sounds can be heard and no pulse felt during the comatose and convulsive states Between attacks, the heart beat and pulse may be of normal rate and rhythm and even the electrocardiogram may not show any abnormalities in auriculo-ventricular conduction, as exemplified by the following case:

A male, 26 years old, suffered from an upper respiratory infection. On the third day of his illness, he suddenly developed recurring attacks of fainting and at times complete loss of consciousness with convulsions lasting 1 to 2 minutes I first examined him when he was free from an attack and was frankly at a loss to understand the reason for his attacks. He showed no abnormal neurologic signs and his heart rate was 110 per minute, regular, the sounds were of good quality and the electrocardiogram showed no abnormalities in conduction While I was still at the bedside, he suddenly began to develop cerebral symptoms. His heart then became irregular and soon no heart sounds could be heard and no pulse felt. An electrocardiogram obtained during a second similar attack, a half hour later, showed progressive prolongation of the P-R interval with dropping out of ventricular beats and soon there was a complete absence of ventricular complexes. The patient fully recovered twelve days later. The particular infection from which he suffered evidently had a specific effect on the conduction apparatus.

The author has observed and reported[1] a similar condition in a male 57 years old, following an attack of acute coronary occlusion.

It must be remembered that complete heart block with a ventricular rate of 30 beats per minute or over and in some cases even with a lower rate,

may be well tolerated and the patient may live fairly comfortably many months or years. Only cases with instability of the ventricular rhythm center, resulting in periods of slowing of the heart to less than 10 beats per minute or with transient complete ventricular asystole, present symptoms of cerebral ischemia.

Ventricular Fibrillation: Transient, and recurring ventricular fibrillation, resulting in paroxysmal cerebral ischemia, probably occurs much more frequently than the reported number of cases found in the literature would indicate The author personally observed four cases of transient ventricular fibrillation, three of which were reported elsewhere.[6, 7, 8] In seven other cases, he found only short phases of the arrhythmia in an electrocardiographic study during the onset of death.[9]

The reason why transient ventricular fibrillation is overlooked is that it cannot be recognized clinically, but requires electrocardiographic studies for its detection If tracings were obtained in all cases of sudden transient unconsciousness and convulsions, and before death due to any cause, the condition would undoubtedly be found to be relatively frequent As in ventricular asystole, due to heart block, a person cannot survive ventricular fibrillation more than three to six minutes The longest survival period was six minutes, in the case reported by Schwartz and Jezer.[10] As in heart block, patients with ventricular fibrillation are completely pulseless and although some fibrillatory ventricular contractions occur, no heart sounds can be heard

It is interesting to observe that many cases of ventricular fibrillation occur in conditions of complete auriculo-ventricular block In other words, cerebral ischemia produced by complete heart block may be due, in some cases, to ventricular asystole, in others, to ventricular fibrillation

Sino-Auricular Arrest or Block This condition may produce temporary or even permanent stoppage of the heart with cerebral ischemia, resulting in the same manifestations as in ventricular asystole or ventricular fibrillation It is usually due to some reflex vagal effect on the sinus node This vagal effect is more apt to occur in individuals with heart disease particularly the arteriosclerotic type There is a possibility that a sudden interruption of the blood supply to the sinus node due to occlusion may, in some cases, result in sino-auricular arrest. Harris[11] has demonstrated that prolonged anoxemia in dogs results, in some instances, in sino-auricular block, even if the vagal nerves are cut Magnusson[12] reported three cases of auricular standstill, one caused by quinidine, one by digitalis, and in the third, stoppage occurred spontaneously as a terminal manifestation of coronary disease Sinus arrest is a frequent occurrence in the course of the dying human heart, as reported before,[9] and as recently shown by Stroud and Feil,[13] and experimentally by Harris [11]

Paroxysmal Tachycardia, Auricular Flutter and Fibrillation: These conditions may produce manifestations of transient cerebral ischemia. Coma and convulsions rarely occur in such cases. In most cases, the manifestations are mild. However, an occasional case of recurring paroxysmal tachycardia may occur where the onset was associated with severe dizziness, loss of consciousness and rarely convulsive movements. The following is an example:

A female, 58 years old, developed recurring attacks of dizziness, stupor, coma and convulsive movements of the extremities, predominantly the upper During one of these attacks, the doctor in charge could not feel the pulse and could hardly hear any heart sounds which recurred at an extremely rapid rate He gave her adrenalin but the symptoms became aggravated and more prolonged An electrocardiogram obtained between attacks showed a regular sinus rhythm with frequent auricular premature contractions. The author therefore suspected that the attacks were in the nature of auricular paroxysmal tachycardia. This was corroborated by tracings obtained during an attack. Prolonged use of quinidine sulphate stopped the attacks

This case illustrates the importance of proper diagnosis of the different forms of cerebral ischemia Ventricular asystole or complete cardiac standstill may be helped by adrenalin but will be aggravated by quinidine.

In a series of 104 cases of paroxysmal tachycardia, Barnes[14] observed cerebral symptoms such as fainting, loss of consciousness, epileptic seizures, visual disturbances and vertigo in fifteen cases. These were most frequent in individuals with cerebral arteriosclerosis.

The cerebral symptoms in the tachycardias occur most frequently in those cases where the ventricular rate is extremely rapid, above 200 beats per minute With slower rates there may be some dizziness and other mild cerebral disturbances, but no coma or convulsions.

Paroxysmal Cerebral Ischemia of Vasovagal Origin

This condition is observed in individuals who present marked sensitivity of the autonomic nervous system These individuals may at one time show symptoms characteristic of a sympatheticotonic state such as tachycardia, elevated arterial pressure, flushing, nervousness and tremors of the fingers At another time, they present symptoms characteristic of a vagotonic state such as marked bradycardia, sweating, drop in blood pressure, and so on. Many of the cases usually show the effects of overactivity of different parts of the sympathetic and parasympathetic systems at the same time.

The mechanism of the production of cerebral ischemia in these cases may consist of sudden extreme slowing or complete stoppage of the heart by

reflex vagal effect or sudden drop in blood pressure by peripheral vasodilatation. In sensitive individuals, fainting caused by some unpleasant sight or bad news is based on these mechanisms.

Cotton and Lewis[15] observed complete stoppage of the heart caused by sino-auricular standstill due to marked vagal inhibition under such circumstances. They proved the vagal origin of the cardiac stoppage by the use of atropin which prevented the attacks Wedd and Wilson[16] observed a case presenting an extreme degree of nodal rhythm with periods of prolonged cardiac standstill and syncopal attacks due to vagal hyperactivity, induced by psychic factors The condition was relieved by atropin Eichna and co-workers[17] observed a case of a young, healthy soldier who developed sinus arrest resulting in cardiac standstill for nineteen seconds, following an episode of hard physical work.

debilitating disease. According to Stead and Ebert[18] it may also occur in disease of the sympathetic nervous system, and Ellis and Haynes[19] observed it in some syphilitic diseases of the central nervous system.

Many cases presenting the Adams-Stokes syndrome are recorded in the literature due to cardiac standstill resulting from vagal irritation by tumors or other conditions. Weiss and Ferris[20] reported a case of diverticulum of the esophagus in which the syndrome was caused by swallowing There are cases reported where the syndrome occurred as a result of various lesions in the brain stem close to the vagal nucleus, such as tumors, local inflammations, varices and so on Fracture of the skull and intracerebral pressure due to any cause may produce similar vagal irritation.

Paroxysmal Cerebral Ischemia of Carotid Sinus Origin

The various vasovagal reactions may occur in some individuals as a result of hyperactivity of the carotid sinus reflex This reflex has been known for hundreds of years to produce unconsciousness. According to Ask-Upmark,[21] the Assyrians used it to dull pain during the rites of circumcision It is only within recent years, however, that the mechanism of unconsciousness resulting from this reflex has been elucidated, mainly by experimental work of Hering[22] and Heymans[23] These authors have demonstrated the afferent and efferent pathways of the reflex and its mode of action

The carotid sinus reflex is carried on by a set of nervous structures, the main sensory receptors of which are located in characteristic manisci, in the adventitia of the pouched out portion of the internal carotid artery at its junction with the external carotid These sensory receptors emerge as

Paroxysmal Tachycardia, Auricular Flutter and Fibrillation: These conditions may produce manifestations of transient cerebral ischemia. Coma and convulsions rarely occur in such cases In most cases, the manifestations are mild However, an occasional case of recurring paroxysmal tachycardia may occur where the onset was associated with severe dizziness, loss of consciousness and rarely convulsive movements The following is an example:

A female, 58 years old, developed recurring attacks of dizziness, stupor, coma and convulsive movements of the extremities, predominantly the upper. During one of these attacks, the doctor in charge could not feel the pulse and could hardly hear any heart sounds which recurred at an extremely rapid rate He gave her adrenalin but the symptoms became aggravated and more prolonged. An electrocardiogram obtained between attacks showed a regular sinus rhythm with frequent auricular premature contractions The author therefore suspected that the attacks were in the nature of auricular paroxysmal tachycardia. This was corroborated by tracings obtained during an attack. Prolonged use of quinidine sulphate stopped the attacks

This case illustrates the importance of proper diagnosis of the different forms of cerebral ischemia Ventricular asystole or complete cardiac standstill may be helped by adrenalin but will be aggravated by quinidine.

In a series of 104 cases of paroxysmal tachycardia, Barnes[14] observed cerebral symptoms such as fainting, loss of consciousness, epileptic seizures, visual disturbances and vertigo in fifteen cases These were most frequent in individuals with cerebral arteriosclerosis

The cerebral symptoms in the tachycardias occur most frequently in those cases where the ventricular rate is extremely rapid, above 200 beats per minute. With slower rates there may be some dizziness and other mild cerebral disturbances, but no coma or convulsions

Paroxysmal Cerebral Ischemia of Vasovagal Origin

This condition is observed in individuals who present marked sensitivity of the autonomic nervous system. These individuals may at one time show symptoms characteristic of a sympatheticotonic state such as tachycardia, elevated arterial pressure, flushing, nervousness and tremors of the fingers At another time, they present symptoms characteristic of a vagotonic state such as marked bradycardia, sweating, drop in blood pressure, and so on. Many of the cases usually show the effects of overactivity of different parts of the sympathetic and parasympathetic systems at the same time.

The mechanism of the production of cerebral ischemia in these cases may consist of sudden extreme slowing or complete stoppage of the heart by

receptor innervations were found in other parts of the vascular tree which respond to intra-arterial blood pressure changes. Sudden increase in arterial blood pressure stimulates the receptor organs in all locations and results in a flow of afferent impulses to the brain stem resulting in vasodepression, cardioinhibition, some alteration in respiration, a decrease in epinephrine secretion and so on, resulting in a lowering of the blood pressure and slowing of the heart. A marked decrease in the intra-arterial pressure produces the opposite effect

The various carotid sinus reflex effects may also be elicited by compressing the carotid sinus region with the finger. In many normal individuals such compression may produce a slight to moderate drop in arterial pressure, slowing of the heart, slight respiratory disturbances and mild cerebral symptoms as dizziness, visual disturbances and so on. In individuals with a hyperactive carotid sinus reflex, the effects may be very alarming. There may be marked slowing or complete stoppage of the heart for variable periods of seconds to minutes, a profound drop in arterial blood pressure, marked respiratory and severe cerebral disturbances culminating in coma and convulsions The types and degrees of response differ in various individuals Some may show predominantly cardioinhibition, others, vasodepression, still others, cerebral disturbances and so on The incidence and degrees of various reactions have been discussed more fully in previous reports[26, 27, 28]

The various cerebral disturbances, including coma and convulsions, induced by the carotid sinus reflex, according to Ferris, Capps and Weiss[29] may occur in occasional cases without stoppage of the heart or profound drop in pressure. In such cases, it is evidently due either to a direct spastic effect on the cerebral vessels or to an effect on the cerebrum itself The slowing or stoppage of the heart when it occurs may be due either to sinus slowing or arrest or to auriculo-ventricular block with various other associated disturbances as described in a previous communication[30]

A hyperactive carotid sinus reflex occurs with greatest frequency in individuals over 40 years of age and particularly in those who present evidence of coronary and cerebral arteriosclerosis This condition sensitizes the individual, apparently, by altering the synaptic connections of the various neurons involved in the reflex

Unconsciousness and Convulsions Due to Other Causes

Many toxic states as well as disease of the central nervous system may be associated with attacks of cerebral disturbances, unconsciousness and convulsions not unlike those caused by paroxysmal cerebral ischemia. In most cases, the differential diagnosis is simple. In some, there may be difficulty.

The more common conditions in which unconsciousness and convulsions may occur are epilepsy, uremia, irritative lesions of the brain such as those caused by hemorrhage, inflammation, abscess, intracranial neoplasm or an aneurysm of a cerebral vessel. False attacks may be observed in hysteria and malingering.

In epilepsy, both the minor and major types, there is usually a history of attacks for years. The major type is preceded by an aura for a few seconds, then the patient cries out and falls to the ground in tonic spasms followed by tetanic convulsions and foaming from the mouth. There are no changes in the heart rate or rhythm during the attack which could account for the manifestations.

In uremia, there is clinical evidence of advanced renal disease as hypertension, cardiac hypertrophy, retinal changes, recurring headaches, anemia, albuminuria and the characteristic uremic odor of the breath. The patient is usually continually comatose between convulsive seizures.

It must be understood, that in occasional cases of uremia, there is also a cardiovascular element which may be an additional factor in the production of unconsciousness and convulsions.

In *irritative conditions of the brain*, there are, as a rule, some signs and symptoms of the underlying disease which help in the differential diagnosis. These vary with the extent and location of the given pathologic process. Here we must emphasize the fact that in those cases where there is marked increase in the intracranial pressure or where the regions of the vagal nuclei are involved, extreme bradycardia, and at times, even cardiac standstill may occur. In such cases the condition may be mistaken for primary cardiac disease. The bradycardia, if extreme, may also contribute to the attacks of unconsciousness and convulsions. The distinguishing feature between primary cerebral ischemia caused by cardiac disease and that caused by a vagal cardio-inhibitory affect induced by the cerebral disease, is that no focal signs of nervous system involvement remain after the attack of unconsciousness and convulsions is over in the former condition.

In hysteria and malingering no true unconsciousness occurs. There is merely a faint attempt to reproduce such a condition and whatever convulsive movements there may be are more or less purposive. Pressure upon the supraorbital notch causes withdrawal of the head. No changes in the heart rate or drop in blood pressure occur.

Treatment

The treatment of the syndrome of syncope and convulsions with the associated manifestations due to paroxysmal cerebral ischemia, depends upon the underlying physiologic disturbance which causes such ischemia. What may be of help in one case may be detrimental in another.

In all cases, the primary aim should be to prevent the onset of acute attacks. This means a careful determination, and the removal, if possible, of the underlying pathologic process which is responsible for the physiologic disturbance. In many cases the pathologic process can not be removed, but the physiologic disturbances may often be stopped or diminished by appropriate therapy, some of which has been described in Chapter VII. If drugs such as digitalis or quinidine are the underlying causes, their use should be discontinued.

The treatment of the acute episode calls for energetic measures to be carried out very urgently. Unfortunately, many cases do not respond to therapy during one or another of these attacks, and death may occur. Others may, perhaps, succumb to the therapy itself.

If the cerebral ischemia is due to ventricular asystole caused by sudden onset of complete auriculo-ventricular block, without the development of a new idioventricular pacemaker, or to sudden cessation of activity of such a pacemaker, urgent medication is necessary in an attempt to establish and maintain a new pacemaker. The best and most reliable drug for that purpose is epinephrine hydrochloride. This should be given in doses of 0.25 to 1 cc. of the 1–1,000 solution, either subcutaneously, intravenously or intracardially, depending upon the urgency of the case.

The subcutaneous method is used in the mild and frequently recurring cases. When this route of administration is used, it is essential to massage the area of injection from time to time to help absorption. This is very essential because adrenalin produces local vasoconstriction which interferes with proper absorption.

The intravenous route is used in cases where ventricular stoppage lasted about one minute or more. The drug should be injected very slowly in any of the superficial veins of the arm. If a response occurs before the full dose is injected, the balance may be withheld.

The intracardiac injection is best reserved for those cases where ventricular stoppage lasted two or more minutes, and where there is fear that the patient will not recover. A 3 inch needle is used for that purpose. The injection is made in the fourth left interspace, a little distance away from the sternal margin. The needle is plunged in to a depth of about 2 inches.

Repeated administration of the adrenalin may be necessary in many cases. Some may require a subcutaneous injection every hour or two in small doses to maintain the effect of the drug.

Inasmuch as adrenalin chloride has been found to produce ventricular fibrillation in occasional cases, and the latter arrhythmia may occur in complete heart block, the drug in itself is dangerous. Its effect should be watched very carefully and, if possible, electrocardiographic studies should be made soon after its administration and followed for some time.

This is true, particularly, when the intravenous and intracardiac routes are used.

Other drugs have been used in this condition, such as ephedrine, barium chloride, thyroid extract and atropin, in an attempt to prevent recurring attacks These have been found to be practically valueless

In 1939 the author reported[5] apparently favorable results in four cases of the Adams-Stokes syndrome by the use of intravenous hypertonic glucose solution Later experiences with this method of therapy left some doubt in his mind as to its definite effectiveness. For, it must be realized that many patients who do not succumb to an attack, often recover spontaneously from an acute episode. For this reason, the value of any medication or treatment may be questioned However, 50 to 100 cubic centimeters of a 50 per cent glucose solution given intravenously and repeated two or three times during the day should be tried Moore and Stewart[31] lar block in a case of

of our available drugs has been unsuccessful The use of quinidine sulphate has been suggested by Levine,[32] Escamilla,[33] Dock[34] and other authors Inasmuch as this arrhythmia often occurs in cases of complete heart block, it would appear that its use would add further hazards to the case. Schwartz and Jezer,[35] Davis and Sprague[36] and other authors found that the drug induces ventricular fibrillation in some cases Inasmuch as spontaneous remissions of attacks of ventricular fibrillation are occasionally known to occur, it is again questionable if the remission of an attack is the result of any drug

In sino-auricular block, Tr belladonna in doses of 1 cc. every four hours by mouth or atropin sulphate $\frac{1}{60}$ to $\frac{1}{75}$ grain may be given intramuscularly or intravenously. The underlying cause must be looked for and if possible removed. Inasmuch as digitalis and quinidine are often the causes, these drugs shoud be discontinued at once.

The management of paroxysmal tachycardia, auricular fibrillation, and auricular flutter *has been fully described in Chapter VII.*

The management of vasovagal syncope depends upon the underlying physiologic process causing the disturbance. Where it is predominantly due to sino-auricular slowing or standstill, belladonna or atropin are the drugs of choice, and should be administered as in other conditions of sino-auricular block. If due predominantly to a fall in pressure, ephedrine sulphate may be given by mouth in doses of $\frac{1}{4}$ to 1 grain every four hours Small doses of adrenalin may be used when symptoms are very acute. Orthostatic hypotension may also respond to such therapy. Benzedrine, 10 to 20 milligrams may be found more valuable in the latter cases.

In syncope and convulsions due to a hyperactive carotid sinus reflex,

the underlying physiologic disturbance responsible for the symptoms must be determined. When stoppage of the heart is the main cause, belladonna or atropin should be used as in any form of sino-auricular block. This will be of help, also, in ventricular asystole due to auriculo-ventricular block induced by this reflex, as the block in such cases is of vagal origin. Where the syncope is due mainly to drop in pressure, ephedrine or adrenalin is to be used In fact, the latter drug is useful in the hyperactive carotid sinus reflex, regardless of what the mechanism of syncope may be.

The most important therapy is to remove any condition that may irritate the carotid sinus The patient must not wear a high collar, and must not bend or stretch his head suddenly In very severe cases, novocain injection in the wall of the sinus may give relief Surgical stripping of the sinus and adjacent portions of the carotid artery of their nerve connections may give relief in occasional cases.

Mechanism of Death

In speaking of clinical death in the complex animal organism such as the human being, we usually refer to the time of cessation of respiration and of the blood circulation Actually, however, life does not completely cease in toto at that time. Some portions of the body remain alive for variable periods of minutes or longer after clinical death. Likewise, portions of the body may be dead, as determined by anatomico-pathologic changes, for variable periods before the organism as a whole dies From a clinical viewpoint, however, we must consider a person dead when the circulation and respiration have ceased long enough to produce irreversibly destructive changes of the vital centers of the brain.

The mechanism of death is still largely in the realm of theorization This is true, particularly, of sudden death often observed in cardiac disease In many such cases, the primary cause of death is probably either sino-auricular arrest, ventricular asystole or ventricular fibrillation, as described before, producing acute cerebral ischemia. In others, the primary cause is probably paralysis of the respiratory or circulatory centers of the brain In both, the acute forms of death as well as in death following prolonged and slow failure of the circulation or respiration, anoxia of the medullary centers of the brain are the underlying causes, regardless of what the mechanism of the anoxia may be.

The interesting experimental work reported by Negovski[4] throws some light on the pathology. In exsanguination experiments on dogs and in resuscitation, they found that the higher centers of the brain die earlier than those portions of the central nervous system without which life is impossible, such as the medullary centers In other words, those portions which are phylogenetically the primitive parts of the central nervous sys-

tem survive longer than the more recent higher centers, and in resuscitation recover earlier The action currents of the cortex are abolished before the disappearance of the eye reflexes and represent the earliest symptoms of cerebral death

Histologic studies of the brain in animals that were revived 6 to 20 minutes after clinical death showed irreversible changes The nerve centers showed vacuoles, hydropic degeneration, chromatolysis, shrinkage and ghost cells Hemorrhages were present at the base of the pons, and the stem and cerebellum showed complete disappearance of the Purkinje cells Marked changes were also found in the cord. Dogs revived 5 to 6 minutes after clinical death showed much less changes, and most of these were reversible

Clinically, we also find that in the majority of cases, the portions of the brain which are of more recent development phylogenetically, having to do with thinking, orientation and higher sensitivity, usually disappear in the process of death much earlier than the primitive portions controlling the circulation, respiration, the metabolic activities and so on. Unconsciousness usually precedes actual clinical death by a variable period. In fact, in some cases, it may continue for days before the cessation of the circulation and respiration

REFERENCES

1 Morgagni, quoted by Pletnew Der Morgagni Adams-Stokessche Symptomen-Komplex Ergebn d inn med u Kinderh 1 47, 1908

2 Adams, R Cases of diseases of the heart Dublin Hospital Reports 4 353, 1827

3 Stokes, W Observations on some cases of permanently slow pulse Dublin Quart J M Sc 2 73, 1846

4 Negovski, V A Agonal states and clinical death Problems in revival of organisms Am Rev Soviet Med 3 339, 1946

5 Sigler, L H Treatment of the Stokes-Adams syndrome by hypertonic glucose solution given intravenously Ann Int Med 13 101, 1939

6 —— Adams-Stokes syndrome induced by transient recurrent ventricular fibrillation Am Heart J 16 109, 1938

7 —— The fibrillatory phase of transient recurring ventricular fibrillation International Clin 1 22, 1938

8 —— Case of ventricular fibrillation following acute coronary occlusion New York State J Med 40 218, 1940

9 ——, Stein, I, and Nash, P I Electrocardiographic changes occurring at death Am J M Sc 194 356, 1937

10 Schwartz, S, P, and Jezer, A Transient ventricular fibrillation The clinical and electrocardiographic manifestations of the syncopal seizures in a patient with A-V dissociation Arch Int Med 50 450, 1932

[illegible] al anoxia, coronary [illegible]

[illegible] enty-three cases reported and a review of the literature Am Heart J 35 910, 1948.

[14] Barnes, A R Cerebral manifestations of paroxysmal tachycardia Am J M Sc 171:489, 1926

[15] Cotton, T F, and Lewis, T Observations upon fainting attacks due to inhibitory cardiac impulses Heart 7 23, 1918–20

[16] Wedd, A M, and Wilson, D. C. Standstill of the heart of vagal origin Am Heart J 5 493, 1929–30

[17] Fichna, L. W, Horvath, S M, and Bean, W B Cardiac asystole in a normal young man following physical effort Am Heart J 33 254, 1947

[18] Stead E A, Jr, and Ebert, R V Postural hypotension, a disease of the sympathetic nervous system Arch Int Med 67 546, 1941

[19] Ellis, L B, and Haynes, F W. Postural hypotension with particular reference to its occurrence in diseases of the central nervous system Arch Int Med 58 773, 1936

[20] Weiss, S, and Ferris, E B Adams-Stokes syndrome with transient complete heart block of vasovagal reflex origin Arch Int Med 54 931, 1934

[21] Ask-Upmark, E The carotid sinus and the cerebral circulation Acta psychiat et neurol, 1935, supp 6, p 1

[22] Hering, H E Karotissinusreflexe auf Herz und Gefasse Dresden, Theodor Steinkopff, 1927

[23] Heymans, C Le sinus carotidien et les autres zons vasosensibles reflexogenes London, H K Lewis & Co, 1929

[24] Brauecaer, W Das pressorezeptorische Nervenssystem und seine praktische Bedeutung in der Chirurgie Beitr z klin, Chir 158 309, 1933

[25] Daly, I D, and Verney, F B The localization of receptors involved in the reflex regulation of the heart rate J Physiol 62 330, 1927

[26] Sigler, L H Further observations on the carotid sinus reflex Ann Int Med 9 1380, 1936

[27] —— Hyperactive vasodepressor carotid sinus reflex Arch Int Med 70 983, 1942

[28] —— Subjective manifestations of the hyperactive carotid sinus reflex Ann Int Med 29 687, 1948

[29] Ferris, E B, Capps, R B, and Weiss, S Carotid sinus syncope and its bearing on the mechanism of the unconscious state and convulsions Medicine 14 377, 1935

[30] Sigler, L H Electrocardiographic observations on the carotid sinus reflex Am. Heart J 9 782, 1934

[31] Moore, N S and Stewart, H J The disappearance of intraventricular heart block occurring in uremia following the intravenous injection of hypertonic glucose solution Am Heart J 5 469, 1929–30

[32] Levine, H D Effect of quinidine sulphate in inhibiting ventricular fibrillation Arch Int Med 46 808, 1932

[33] Escamilla, R F Report of a case of paroxysmal ventricular fibrillation in relation to quinidine therapy Am Heart J 8 850, 1932

[34] Dock, W Transitory ventricular fibrillation as a cause of syncope and its prevention by quinidine sulphate Am Heart J 4 709, 1928–29

[35] Schwartz, S P, and Jezer, A The action of quinine and quinidine on patients with transient ventricular fibrillation Am Heart J 9 792, 1933–34

[36] Davis, D, and Sprague, H B Ventricular fibrillation Its relation to heart block Am Heart J 4 559, 1929

CHAPTER XVI

Shock: The Syndrome of Hemostasia

FAR, we have described failure of the circulation due to abnormalities or disease of the heart. Such failure may be said to be of central ori-

In this chapter, we shall attempt to describe failure due primarily to :tional abnormalities of the arteriolo-capillary-venular system This lition may be spoken of as circulatory failure of peripheral origin If :t failure ensues here, it is secondary to insufficient return of blood from periphery towards the heart.

he manifestations of this form of failure are covered by the all-inclusive ı "shock" Although this term fails to give any hint of the fundamen- vascular phenomena, we will, nevertheless, retain it because of its long universal usage

'efinition of Shock Shock may be defined as a state of general anoxemia, xia and toxemia associated with hemostasia in the capillary and venular cals of the vascular system induced by severe bodily trauma or emotional ırbances and exhibiting itself in characteristic pathologic changes and cal manifestations.

onditions Producing Shock In animal experimentation, shock may be luced by section of the spinal cord, by tight tourniquets applied to the l limbs for several hours and then releasing them, by scalding the body ı boiling water, by prolonged general anesthesia, by injecting macerated ıes and by various other means. In some animals, such as the rabbit re there is an inadequate compensatory mechanism present for the 'ity effect on the circulation, the mere assumption of the erect posture a certain period of time will result in shock

ı the human, shock may likewise occur in very severe bodily injuries to any cause, in surgical operations having a combined effect of the :sthesia, manipulation and traumatization of the body tissues, in severe ıs of the body surface and in perforation of a viscus.

here are many other diseased states of the body which may result in eater or less degree of shock In some, shock is a terminal manifesta- . Most of these belong to the category of medical rather than surgi- :onditions Of these may be mentioned embolization and thrombosis arious vascular regions, the complicating and terminal states of certain

mic states, overdosage of various drugs, particularly the barbiturates; and various severe infectious and intoxicating states where it may occur mainly as a terminal manifestation.

Severe forms of shock may also occur in some individuals as a result of grave emotional upset such as experiencing horrible events or sights on the battlefronts in war. Many of these cases may develop symptoms of shock after they have been removed from the actual place of horror. These individuals undoubtedly have a constitutional inferiority of the nervous system affecting the control of the vascular apparatus.

Broadly speaking then, shock may be said to be induced by any trauma of great enough magnitude to upset the normal circulatory balance of the individual The trauma may be of extrinisc, intrinsic or psychic origin The reactivity of the individual to trauma varies. The same amount of trauma that may result in fatal shock in one case, may produce comparatively little or no shock in another.

Clinical Manifestations These depend upon the degree of shock, its duration and whether or not it responds to therapy, that is, whether reversible or irreversible. In the former, shock is at no time as profound as in the latter.

A mild form of shock may pass unnoticed and only careful physical examination may detect its presence More severe grades present marked pallor mixed with a tinge of cyanosis which gives the patient an ashen color His skin is moist and cold. He usually lies calmly although at times he is markedly restless and fidgety, especially if the condition causing the shock is associated with severe pain Superficially, he usually looks apathetic, although from all appearances he is quite concerned and extremely [illegible]

by coma from which the patient cannot be aroused

The musculature of a patient in shock is flabby and relaxed. Voluntary muscular movements are almost abolished and the reflexes are greatly diminished. The respiratory rate is usually slow and deep but occasionally it may be accelerated and irregular In severe cases, Cheyne-Stokes breathing may occur.

In the majority of cases the heart rate is greatly increased, although in occasional cases, it may be diminished The heart sounds in the early phases may be louder than normal, although in the later phases, especially in the irreversible type, they become greatly diminished and hardly audible. At this stage, a gallop rhythm may develop and a faint systolic murmur may be heard over different areas of the precordium which further muffle the sounds The pulse is rapid, corresponding to the heart rate and is of very small amplitude, very weak and from time to time, imperceptible. In

the irreversible form it usually remains persistently imperceptible till the end The character of the pulse thus is not in conformity with the intensity of the heart sounds

The arterial blood pressure corresponds to the amplitude of the pulse. When imperceptible, the blood pressure is, of course, not determinable. When perceptible, it may vary between 50 and 90 millimeters systolic and 40 to 70 diastolic In the milder cases, the systolic pressure may be higher than 90 and if previous hypertension was present, it may reach as high as 120 or even higher, in the early phases

The venous pressure in shock is greatly diminished and in the severe, irreversible form may be zero, the veins remaining almost entirely collapsed In many such cases, it is often impossible to draw blood from any of the *larger superficial veins*

The digestive processes are curtailed and a variable degree of abdominal distention occurs due to paralytic ileus. Vomiting and great thirst are often present. The sphincteric control is diminished and involuntary defecation may occur in the late stages

Renal excretion is markedly diminished In the irreversible form, it *may entirely stop till the end The nitrogenous products of the blood are* thus not fully excreted, resulting in nitrogen retention.

Physiologic Mechanism The underlying physiologic changes that may be responsible for the clinical manifestations of shock have been the subject of experimental investigation and extensive theorization for many years Many of the theories have been based only on fragmentary observations and do not explain the basic pathologic changes and clinical findings These will be left out of our discussion We will present here only certain experimental and clinical observations which when taken together, will give us some theoretical background of the physiologic mechanism of shock.

The main factor that attracted the attention of early experimenters was the marked drop in arterial blood pressure This was thought to be due to the universal loss of tone of the vasoconstrictor nerves to the arterioles. Morrison and Hooker[1] have demonstrated, however, that the vasoconstrictor mechanism in shock is intact In fact, Henderson[2] has shown that *there is a compensatory increase in vasoconstriction in shock to prevent* too much of a drop in blood pressure in the early stages. This was also observed by Erlanger and co-workers[3] The reflex vasoconstriction is protective in nature, being an attempt to maintain a proper blood supply *to the heart and* to the vital centers of the brain, particularly the respiratory center.

That there is vasoconstriction in shock is evidenced clinically from marked pallor that the patient presents. Freeman and co-workers[4] have shown that vasoconstriction is more marked in the peripheral portions of

the body than in the central areas Kondo and co-workers[5] found a decline and cessation of blood flow in the forepaw in experimental shock in animals before the systemic blood pressure falls. The central areas of the body also share considerably in the vasoconstriction. Thus, Lauson and co-workers,[6] in a study of the urea clearance in 35 cases of shock, found the rate of glomerular filtration to be greatly reduced The reduction was out of proportion to the reduced general arterial pressure. This suggests the presence of active renal vasoconstriction. The vasoconstriction is also partly responsible for the oliguria and anuria observed in shock They believe that the renal ischemia probably augments the acidosis of shock.

Inasmuch as there is a fall in arterial blood pressure in the face of universal vasoconstriction, we must conclude that diminished cardiac output is responsible for such a fall This has been shown to be due to decreased diastolic filling of the heart caused by insufficient venous return. Kondo and Katz[7] have demonstrated a consistent decline in the size of the heart in shock due to loss of the circulating blood volume

The loss of circulating blood volume or oligemia has been demonstrated to be due to emptying of the blood into the capillary and venular radicals and to the escape of plasma in various parts of the body particularly in the splanchnic area Gasser and co-workers[8] observed that the capillaries and the small veins in the intestinal mucosa were markedly dilated and tightly packed with blood cells in shock. The latter was due to the escape of plasma. Cannon and co-workers[9] have also observed concentration of the stagnated blood in the capillary radicals due to the same cause.

That universal capillary permeability occurs in shock, has been recently questioned by Fine and Seligman[10] and Noble and co-workers[11] who claim to have found no experimental evidence of change in the permeability of the generalized capillary bed They observed the escape of plasma and blood corpuscles only in traumatized areas Fox and Keston[12] in a study of the distribution of radioactive sodium in experimental shock observed a great accumulation and side-tracking of sodium in injured tissue. Moon[13] in a pathologic study has demonstrated, however, the occurence of widespread capillary exudation in experimental and clinical shock

The cause of capillary and venular stagnation of blood is still not definitely known The work of Dale and Richards[14] throws some light on the possible effect of some toxic products of the traumatized tissue as the cause These authors found that histamin injection in normal animals produces shock by capillary dilatation This occurs much more readily under the effect of ether and is true also of shock in the human. It is possible that some histamin-like product is being formed by traumatized tissue which enters the circulation and produces capillary paralysis The exact nature of such a product, if indeed present, is not known. The presence of aci-

dosis in shock suggests the possibility that lactic acid may be a cause but injection of large amounts of this material in animals failed to bring about this phenomenon.

The recent work of Shorr and co-workers[15] appears to have demonstrated a specificity of various humoral substances in the pathogenesis of capillary stasis. These authors based their observations on the work of Chambers and associates who found that shock consists of two phases, an initial compensatory and a subsequent decompensatory phase. The compensatory phase consists of intermittent constrictor activity of the mesarterioles and precapillary sphincters and heightened reactivity to epinephrine. The hyporeactive or decompensatory phase consists of progressive depression of the terminal arterioles and precapillaries resulting in overflowing of the capillary bed, progressive venular stagnation and failure of venous return That both phases are caused by some humoral element was shown by the fact that injection of blood from traumatized rats to normal ones produced the same vascular effects in the latter as in shock

Shorr and co-workers made saline extracts of the tissues of various organs from animals in shock They found that kidney extracts yielded vasoconstrictor material while liver and skeletal muscle yielded vasodilator material if extracts were obtained during the decompensatory phase They believe that tissue anoxia due to reduced oxygen transport in shock was the likely explanation of the production of these materials They have therefore made extracts of normal liver, skeletal muscle and kidney which were previously exposed for some time to an atmosphere of 5 per cent oxygen and 95 per cent nitrogen. Injection of these materials in normal animals produced the same effects as the injection of extract of the same organs obtained from shocked animals This tends to prove that tissue anoxia results in humoral substances which have different effects in ultimately producing distention and stasis of the capillaries and venules.

Besides a possible humoral element, a marked diminution in intramuscular pressure due to complete muscular relaxation as a result of loss of nervous power is probably a factor in the production of capillary and venular stasis. It has been shown in Chapter IV that the venopressor mechanism of muscular activity is greatly responsible for the emptying of the venular radicals into the veins and the propulsion of the venous blood towards the heart. The effect of anesthesia in precipitating or in aggravating a state of shock is perhaps at least partly due to complete muscular atony it produces. Henstell and Gunther[16] believe that a lowered level of intramuscular pressure is more responsible for peripheral vascular failure than diminished plasma volume of the blood Previously, Gunther and co-workers[17] demonstrated that after fifty minutes of continuous surgery, a drop in intramuscular pressure may precede the fall in venous pressure. The intramuscular pressure fell five minutes before a shocklike state began.

From an analysis of the available data presented above, we may conclude that the shock syndrome is probably caused by the following sequence of abnormal physiologic events: As a result of a sudden overwhelming of the nervous system by traumatic onslaught, muscular atony occurs. This causes an interference with the forward propulsion of blood towards the heart by the failure of the venopressor mechanism Stagnation of blood in the capillary bed results. In nature's attempt to save the vital centers of the body, universal arteriolar vasoconstriction occurs which temporarily prevents an extreme drop in arterial pressure. This in turn, further slows the circulation through the capillary system. The diminished propulsion of blood towards the heart results in decreased diastolic filling of the heart, therefore a diminished emptying into the arterial system. Tissue anoxia soon follows, producing perhaps some humoral element or elements which cause capillary and venular dilatation and further stagnation of blood as well as some capillary injury. Exudation in the tissue spaces takes place due to such capillary injury, resulting in hemoconcentration and still further stagnation The total circulating blood volume is thus markedly reduced, resulting in a further diminution in volume flow Complete failure of the circulation soon occurs, including also failure of the heart because of insufficient coronary supply and insufficient intraventricular pressure.

It must be understood that, although the shock syndrome may be approximately the same, whatever the underlying cause may be, the mechanism undoubtedly varies to some extent in different cases This has recently been suggested by Hechter and co-workers [15]

Pathology: The pathologic changes induced by shock in various parts of the body have been studied by Moon [13] These consist, in general, of marked engorgement of the capillary and venular radicals of all the organs of the body, resulting in diffuse congestion and somewhat cyanotic appearance of the serous and mucous surfaces Many capillary hemorrhages occur, frequently resulting in blood tinged fluid in various body cavities and in ecchymosis in the internal organs. The lungs may be markedly edematous Degenerative changes of the parenchyma of some of the organs, especially the heart, are often evident.

The large superficial veins are collapsed and bloodless. The blood in the heart and great vessels is thick and not clotted and is often of deep purplish color

The clinico-pathologic findings reported by various authors consist of slight elevation in the blood sugar level in some cases, probably due to the liberation of sugar from the liver as a result of excessive sympathetic activity. Acidosis is a frequent finding probably due to an accumulation of acids, perhaps mainly lactic, due to anoxia. In many cases, especially where there is widespread tissue destruction, there is an increase in the potassium of the blood. Zwemer and Scudder[19] considered an increase in blood

potassium to be a factor in the causation of shock. This has not been proven. Urea nitrogen and creatinine are increased and the basal metabolic rate is markedly reduced The prothrombin time is often prolonged and the icteric index is elevated

Marked hemoconcentration due to a decrease in the plasma volume caused by capillary permeability is one of the most important findings in shock. The red cell count obtained from the capillary bed may reach in advanced cases, as high as 9,000,000 per cubic millimeter and is usually lower in blood obtained from a vein The blood may be so concentrated that cutting the tissues may result in a very slow exudation of thick, dark, viscous material In the earlier and milder stages, the hemoconcentration is not as marked but even at such stages, the red cell count is high It may at times be used as the main criterion of the presence of shock, before other profound manifestations are present

Differential Diagnosis: Shock must be differentiated from hemorrhage and the late stages of congestive failure.

Massive hemorrhage may produce a clinical picture similar to shock. Indeed, bleeding has been used experimentally as a method of producing the shocklike state and the findings are often described interchangeably with those of shock due to trauma This is particularly true in clinical cases where internal hemorrhage may result in a mixed picture of hemorrhage and shock, the latter being due to irritation and absorption of the hemorrhagic blood

There are certain basic differences between hemorrhagic and traumatic shock. In hemorrhage, if extremely severe, the color of the patient is blanched, not ashen, the respirations are usually increased in rate and may be sighing A blood count obtained from any capillary bed yields a marked decrease in the number of red cells, due to the fact that the plasma volume is relatively greater than the blood cell volume. This is caused by the compensatory absorption of fluids from the tissues into the capillaries. In shock due to other causes, on the other hand, there is hemoconcentration due to escape of plasma from the capillaries into the tissues Also, according to Moon,[13] on postmortem examination the organs, in the case of hemorrhage, are blanched rather than congested and no exudation is present.

From the *later stages of congestive heart failure*, shock may be easily differentiated by the cyanosis, marked dyspnea and increased venous pressure in the former, in contradistinction to the ashen color and extremely low or zero venous pressure in the latter

Treatment: In the therapy of shock, the main aim should be to prevent its occurrence. If it has developed, an attempt should be made to stop its progress and to return the circulation to normal functional ability.

The prevention of shock in operative cases consists primarily of proper preoperative and operative care, as described in Chapter XXXI. In other cases, there may not be any means of its prevention.

In all cases it is most essential that the condition be recognized in its initial, if possible, preclinical stages, at which time the best results may be expected from therapy.

When the presence of shock has been detected, the primary aim should be the restoration of fluid loss from the capillary tree, and the supply of oxygen in order to overcome the general anoxia. The first calls for massive fluid intake The second calls for artificial supply of a high concentration of oxygen, as described in Chapter XIII.

The administration of fluids in the early and mild cases may be by mouth and by hypodermoclysis, if necessary. In more advanced cases a continuous venoclysis may be employed. The various solutions advocated include normal saline solution, glucose and saline, or solutions of saline with serum albumin, gelatin, or acacia. In many cases the use of blood serum, plasma or whole blood procduces the best results.

Hechter and co-workers[20] believe that it is the sodium ion of sodium chloride in any of the solutions used that produces the therapeutic effect Simple fluid displacement could not explain such affect, for equivalent volumes of isotonic glucose solution are less effective. They also believe that serum is no more effective than equivalent volumes of saline, and the colloidal osmotic activity of gelatin solution has no influence on mortality. They add, however, that this principle applies to scald shock and can not, as yet, be definitely applied to all forms of shock. Moon[13] observed that injections of salt solution produced only transient beneficial effects

Frazier[21] considers the use of 10 per cent ethyl alcohol in 10 per cent dextrose solution given slowly, intravenously to be helpful As much as two liters may be given this way in twenty-four hours The value of dextrose, however, has been questioned by Moon. He pointed out that the blood glucose is already higher than normal in shock, and the low metabolism present here is not due to lack of fuel, but to anoxemia

Stead and co-workers[22] found that 25 per cent solution of human albumin given intravenously produces a satisfactory hemodilution with an increase in blood volume within a comparatively short time. He believes that the ease and rapidity of its administration, its stability and absence of unfavorable reactions make it useful in many emergencies as a substitute for plasma, but not for whole blood

Drug therapy is of no definite value in shock Some drugs may actually be harmful Thus, the use of digitalis is definitely contraindicated and may add toxicity to an already serious state A rapid heart rate and poor heart sounds in this condition are secondary to peripheral vascular failure.

and will not, in any way, be benefited by this drug. This point is stressed because the author has observed several instances where digitalis was used to the exclusion of more rational methods of therapy with fatal outcome Such outcome could be attributed, at least partly, to the toxic effect of the drug That the heart fails in the terminal phases of irreversible shock may be true, but in those phases, no method of therapy is of any avail.

Adrenalin used for the purpose of raising the blood pressure is, likewise, of no value and may, at times, actually hasten a fatal outcome. It must be remembered that this drug produces its effect through peripheral vasoconstriction which is already present in shock and does not in any way influence the basic pathologic process of capillary permeability and loss of fluid and plasma

Adrenal cortical hormone apparently does seem to have beneficial effects in some cases, according to a few isolated reports. It probably acts best in the prevention of shock.

Other drugs, such as caffein, strychnine, and pitressin have no demonstrable value Frazier[21] believes that the last drug may have some value. Where restlessness is marked, morphine is indicated

Holmes[23] observed that vitamin C given pre- and postoperatively is of great help in preventing and allaying shock. He uses 500 milligrams before and after operations

REFERENCES

1 Morrison, R A, and Hooker, D R The vascular tone and the distribution of the blood in surgical shock Am J Physiol 37 86, 1915

2 Henderson, Y Acapnea and shock--Carbon dioxide as a factor in the regulation of the heart rate Am J Physiol 21 126, 1908

3 Erlanger, J, Gesel, R, and Gasser, H S Studies in secondary traumatic shock The circulation in shock after abdominal injuries Am J Physiol 49 90, 1919

4 Freeman, N E, Shaw, J L, and Snyder, J C The peripheral blood flow in surgical shock J Clin Investigation 15 651, 1936

5 Kondo, B, Katz, L N, Meyer, J, and Molinow, M R The plethysmographic measurement of blood flow through the forepaw during experimental shock Am Heart J 33 207, 1947.

6 Lauson, H D, Bradley, S E, and Cournand, A The renal circulation in shock J Clin Investigation 23 381, 1944

7 Kondo, B, and Katz, L N Heart size in shock produced by venous occlusion of the hind limbs of the dog Am J Physiol 143 77, 1945

8 Gasser, H S, Erlanger, J, and Meek, W J Studies in secondary traumatic shock IV. The blood volume changes and the effect of gum acacia on their development Am J. Physiol 50 31, 1919

9 Cannon, W B, Fraser, J, and Hooper, A N Some alterations in the distribution and character of the blood. J A M A 70 526, 1918

10 Fine, J, and Seligman, A M Traumatic shock VII A study of the problem of the "lost plasma" in hemorrhage, tourniquets and burn shock by the use of radioactive iodo-plasma protein J Clin Investigation 23 720, 1944

[11] Noble, R. P., Gregersen, M I, Porter, P. M, and Buckman, A Blood volume in clinical shock II The extent and cause of blood volume reduction in traumatic, hemorrhagic and burn shock J Clin Investigation 25 172, 1946
[12] Fox, C. L, and Keston, A S Mechanism of shock from burns and trauma traced with radiosodium Surg, Gynec & Obst 80 561, 1945
[13] Moon, V H. Shock and Related Capillary Phenomena London, N. Y., Toronto, Oxford University Press, 1938.
[14] Dale, H H, and Richards, A N Vasodilator action of histamine and of some other substances J Physiol 52 110, 1918
[15] Shorr, E, Zweifach, B S, and Furchgott, R F. On the occurrence, sites and modes of origin and destruction of principles affecting the compensatory vascular mechanisms in experimental shock Science 102 489, 1945
[16] *Henstell, H. H, and Gunther, L · Studies of plasma volume in the human being.* Am J. M Sc 209 187, 1945
[17] Gunther, L, Henstell, H H, Strauss, L, and Engelberg, H Intramuscular pressure. IV The venopressor mechanism during the course of surgical procedures Am J. M Sc. 204 394, 1942
[18] Hechter, O, Bergman, H C, Sapirstein, L, Fisk, R, Feigen, G, and Prinzmetal, M · Further studies on the liver principle which is effective against burn shock. Am Heart J. 29 499, 1945
[19] Zwemer, R L, and Scudder, J Blood potassium during experimental shock. Surgery 4 510, 1928
[20] Hechter, O, Bergman, H C, and Prinzmetal, M Comparison of therapeutic effectiveness of serum and sodium chloride in scald shock Am Heart J 29 484, 1945
[21] Frazier, C H The modern treatment of surgical shock J A M A 105 1731, 1935.
[22] Stead, E A, Jr, Brannon, E S, Merrill, A J, and Warren, J V Concentrated human albumin in the treatment of shock Arch Int Med 77 564, 1946
[23] Holmes, H N Use of vitamin C in traumatic shock Ohio State M J 42 1261, 1946

CHAPTER XVII

Arterial Hypertension. Hypertensive Heart Disease. Hypotension

Arterial Hypertension

There is no subject in medicine that has received more attention than arterial hypertension, and yet its main underlying cause or causes are still, more or less, shrouded in mystery

Definition: Arterial hypertension is not a clinical entity, but is merely a physiologic disturbance, like an increase in the body temperature or pulse rate, which occurs under certain abnormal conditions. As such it may be caused by a variety of pathologic states In some cases the underlying pathology is known In the vast majority of cases, comprising the group of so-called essential hypertension, no known causative pathologic process is discoverable

Physiologic Mechanism

The condition may theoretically be induced by an increase in either one or more of the four factors which maintain normal blood pressure, namely the cardiac output, the volume of circulating blood, the viscosity of the blood and the peripheral resistance Of these, an increase in the cardiac output may be a factor in the production of the systolic hypertension associated with aortic insufficiency or in thyrotoxicosis. In so-called essential hypertension, however, it has been demonstrated by Holman and Page[1] and other authors before them, that the cardiac output is the same in the hypertensive as in the prehypertensive state There was also no increase observed in the viscosity of the blood by Austrian[2] and other authors, or in the blood volume by Linder and co-workers.[3] It is, therefore, a greater peripheral resistance which is responsible for the hypertensive state.

According to Wiggers,[4] the peripheral resistance is not the same in all regions of the body at any given time. There is an increased resistance in one location at the same time that passive or active diminution in resistance occurs in other regions. It is the sum total of the various degrees of resistance in the different parts of the body which results in the augmented collective or effective peripheral resistance which causes hypertension The splanchnic region is the area where the greatest peripheral resistance occurs.

The predominant cause of increased resistance is *functional constriction of the arterioles*, not structural disease. This is evidenced by the fact that the blood pressure in hypertension may be temporarily diminished by

certain drugs or by rest. Also, we often see cases with marked general arteriosclerosis without hypertension.

The underlying cause or causes of the arteriolar constriction has been the subject of speculation for many years. Because of the increase in blood pressure under nervous and emotional states, the main attention was focussed upon hyperactivity of the vasomotor system as the possible underlying cause. This hyperactivity was considered to be in the vasomotor center, induced by reflexes from various parts of the body, especially the brain. As a result of the hyperactivity, prolonged vasospasm particularly of the splanchnic area was supposed to occur resulting in the increased resistance. The vasomotor theory is still being adhered to in a modified form, although Tigerstedt and Bergman[5] demonstrated as long ago as 1898 that a humoral substance produced by the kidneys which they named "renin" induced transient hypertension. The vasomotor theory is supported by considerable experimental and clinical evidence. Thus, lesions produced in the midbrain or section of the carotid sinus and aortic depressor nerves result in hypertension, although not persistent. Recently, Fishback and co-workers[6] produced chronic hypertension in dogs by ligating, in series, the arteries supplying the head. Also, spinal anesthesia has long been known to be followed by a fall in pressure. Recently, Gregory and Levin[7] observed a marked drop in blood pressure under high spinal anesthesia, in a series of hypertensive cases, with or without nephritis or uremia.

Stimulated by the illuminating experimental work of Goldblatt and coworkers,[8] the theory of a humoral element as a factor in the production of hypertension has again come to the fore. These authors have produced a persistent type of hypertension experimentally in dogs by prolonged ischemia of the kidneys. This was induced by constricting both renal arteries or one renal artery and the removal of the opposite kidney. The constriction was done by a specially designed adjustable silver clamp. The experimental hypertension resembles essential hypertension of the human, both being unaccompanied in the early stage by a decrease in renal excretory function. In the experimental form, the diminution in the blood flow to the kidneys is caused by a reduction in the lumen of the main artery, while in the human form, it results from lessened flow through the smaller, mainly in the preglomerular arteries. Corcoran and Page[9] believe that renal hypertension may occur even without renal ischemia. Mere reduction in the renal pulse pressure and perhaps moderate reduction in the mean pressure seem to be adequate stimuli.

Goldblatt[10] further demonstrated that experimental hypertension occurred even when all nerve connections of the kidneys were interrupted, or when the kidneys were transplanted to the neck or the groin. He, therefore, concluded that a humoral pressor substance elaborated by the ischemic

kidney, rather than a reflex factor from the kidneys was responsible for the hypertension.

In other experiments, Goldblatt[11] found that he could not produce experimental hypertension in dogs if the adrenal cortices were previously removed, and that well-established hypertension subsided in dogs whose adrenal cortices were later removed This was observed also by Page[12] who suggested that the adrenal cortical secretion maintains the body in a responsive state to a humoral substance produced by the ischemic kidneys. Removal of other endocrine organs, such as the gonads, thyroid, parathyroid and pancreas have no lowering effect on experimental hypertension

Glenn and co-workers[13] observed that if the spinal cord is destroyed below the level of the fifth cervical vertebra after experimental hypertension was induced in dogs, there was a fall in blood pressure below the previous normal level followed by a return to a level above the normal but not to the previous hypertensive state This, as well as the fact that hypertension in the human drops after spinal anesthesia, would indicate that besides a humoral element, the nervous factor is essential for the maintenance of hypertension

We *may conclude from these facts that the humoral element sensitizes* either the vasomotor system or the arteriolar walls to produce hypertension The adrenal secretion is necessary perhaps for the activation of the humoral substance or for sensitizing the effector structures

The nature of the pressor substance produced by the kidneys is not as yet definitely known It was found that repeated injections of renin at short intervals resulted in a diminution of its pressor effects and soon no effect was obtained It is therefore believed that renin itself is not the main pressor factor. Kohlstaedt and co-workers[14] found a pseudoglobulin fraction of the blood which they named "renin activator." This substance interacts with renin forming a new substance, "angiotonin," which is a dialyzable material with strong pressor properties and produces prolonged hypertension. This work was corroborated by Braun-Menendez and co-workers[15] who named the substance "hypertensine." Page and Helmer[16] have shown that the amount of renin activator is increased in dogs with experimental hypertension.

Angiotonin or hypertensine produces the same hypertensive state in animals as essential hypertension in man. According to Page,[17] in both conditions there is no reduction of blood flow to the tissues under its effects, unlike the effects produced by epinephrine or pitressin which produces pallor and a cold skin. Early, there is renal impairment in the concentration of urine in both conditions, long before there is a lowering of urea clearance. Although constriction of the afferent and efferent arterioles to the glomeruli takes place under its effect, the increased systemic pressure results in a normal rate of blood flow through the excretory tissues. Angio-

tonin increases the heart beat and efficiency of the heart muscle. In larger amounts, it produces heart failure. As in essential hypertension in man, the elevation of blood pressure in animals by angiotonin is asymptomatic.

Besides the production of a pressor substance by the ischemic kidney, various observers have found that the normal kidney produces an anti-pressor substance which is greatly diminished in quantity by renal ischemia. This subject has recently been reviewed by Page and co-workers.[18, 19] They have prepared a blood pressure reducing extract from the kidneys which they have found to be of value Goldblatt and co-workers,[20] however, feel that the possibility for a cure of hypertension by this means is not great. At best, it may perhaps relieve the condition temporarily, like insulin in diabetes

Although the recent experimental work enumerated above indicates the possible mechanism of essential hypertension, we are still far from a solution of the problem in the human. If prolonged renal ischemia is the cause of hypertension, what produces this condition in human essential hypertension? If it is persistent spasm of the renal arterioles, what produces this spasm? If it is caused by angiotonin which by its general spastic effects on the arterioles, including those of the kidneys, produces more renal ischemia, and in turn more renin, and thus more angiotonin, what brings about this vicious cycle? If it is an increase in the pseudoglobulin, what physiologic processes increase that substance? These problems are still far from solved

That there is a *hereditary* predisposition to essential hypertension is well attested by every clinician Ayman[21] found an unusually high incidence of hypertension in 1524 offspring of hypertensive families. Hines,[22] in applying the cold pressor test to children of hypertensive parents, found that 95 per cent of the children were hyper-reactors What the inherited factor may be is not known. It may perhaps be an inherited peculiarity in the nervous system which makes it react excessively to any environmental stimulation by increase in vaso-motor response Or, it may also be an inherited constitutional inferiority of the blood vessels, responding to some of the chemical processes of the body by abnormal constriction

That environmental factors also play a great part in the production of hypertension seems to be attested by clinical observations. There is something in our civilization that appears to [illegible]

of the literature, Schulze and Schwab[23] observed that hypertension is almost unknown in native Negroes of Africa while in their descendants in this country, 200 years later, the incidence of hypertensive cardiovascular disease is two and one-half times greater than in native white Americans. They attribute the condition to an emotional, erratic state with an exag-

gerated response to environmental stimuli and lack of restraint. In fear they are panicky, in happiness they are hilarious, in love erotic According to these authors, this mental makeup is not shown by the African Negro.

We have good reason to believe that the hurried and worried life of our civilization, the great tempo with which we move and live, the anxieties, frustrations and artificialities are factors which change the personality and affect the nervous mechanism, controlling the circulation. That psychic factors are operative in temporarily increasing the blood pressure is well known It is highly possible that such factors in certain types of individuals act as permanent stimulating elements of the vasomotor system Moschcowitz[24] found that the greatest proportion of hypertensive patients conforms to a certain type of personality, both physical and psychic Physically, they are soft-muscled, pudgy, short-necked, ungraceful, nonathletic and overweight Psychically, they have no illusions, they do not play, they are irritable and have a single-track mind They are very tense and pursue their aims with a grim desperation He believes that these are the results of our hectic civilization. Ayman[25] described the psychologic makeup of the hypertensive as dynamic, hyperactive with a large steady output of energy, sensitive and quick-tempered From personal experience the author found Ayman's description to apply to the majority of cases, and in many instances the complete description given by Moschcowitz holds true

In a recent analytic study of the personality in 24 patients of essential hypertension, Briger and co-workers[26] found that in every case, there was some serious environmental situation in infancy and childhood resulting in chronic emotional disturbances which were carried to later life

It thus appears that the fundamental causes of essential hypertension in the human are hereditary and acquired characteristics, both of which play their part in the production of vasospasm This vasospastic reaction probably affects, in the early stages, the preglomerular arterioles, resulting in renal ischemia with the production of some humoral substance. This, in turn, results in greater vasospasm, thus perpetuating the vicious cycle. [illegible] stage of normal renal function, appears to have been demonstrated by Smith and co-workers.[27] They found a diminished renal clearance of diatrast, phenol red and inulin in hypertensive, as compared to normal individuals.

Determination and Range

In determining if hypertension exists in a given individual, it is important to rule out a *transient* increase in blood pressure that occurs under strain,

excitement or the use of hypertensive drugs. In some normal individuals, the blood pressure may rise as high as 180 systolic or more, soon after strenuous work or great excitement, but will come down to normal at rest. Adrenalin, ephedrin or benzedrin will temporarily raise the pressure above normal levels

In some sensitive individuals, the rise in pressure may be even higher under similar circumstances and there may often be observed marked spontaneous fluctuations, reaching, at times, above the normal limits, as previously described.[28] In a recent study of the records of 22,741 army officers who showed a transient rise in blood pressure and who were followed over a period of years, Levy and co-workers[29] found that a sustained hypertension occurred more frequently in this group than in individuals showing no transient rise.

Hypertension may be said to exist if repeated determinations, under restful quiescent conditions, show a systolic pressure persistently above 150 and a diastolic above 90 The degree of hypertension is measured by the height above these upper limits of normal. The highest systolic pressure the author has encountered has been above the maximum 300 mm. Hg. limit the usual blood pressure apparatus records, and the highest diastolic was 180 mm. Hg Between the lowest and highest systolic and diastolic levels the figures vary markedly in different hypertensive cases There is also a marked fluctuation in the levels in the same individual from time to time in many cases, as shown in a previous communication.[30] Many hypertensive cases with high blood pressure levels may have periods of normal blood pressure even under the same conditions of rest or activity.

Pathologic Causes

Having determined the presence of hypertension in a given case, it is important to ascertain, where possible, the underlying cause As said before, in the vast majority of cases, no cause can be discovered, and such cases are grouped in the class of so-called *essential hypertension*. In a few other cases, such conditions as thyrotoxicosis, aortic insufficiency, acute or chronic nephritis, unilateral pyelitis or pyelonephritis, increased cerebral pressure due to any cause, adrenal blastoma and so-called Cushing syndrome may explain a hypertensive state. Of these, the last two are of particular interest, although rare

Adrenal blastoma as a cause of hypertension was first reported by Oppenheimer and Fishberg.[31] It is characterized by attacks of paroxysmal rise in blood pressure to as high as 300 mm. Hg systolic and 200 mm. diastolic, in some cases, lasting a few minutes to two days During this period, the patient shows marked pallor followed by flushing, sweating, nausea, palpitation, tachycardia and angiospasm in the fingers In the interval between attacks, the patient usually feels well. Occasionally, the

hypertension remains high also between attacks. The condition is associated with an adrenal tumor which may, at times, be palpable and the symptoms are caused by a hyperadrenalemia.

The syndrome of hypertension together with obesity, hirsuties, amenorrhea, glycosuria, polycythemia, osteoporosis and purplish cutaneous striae, was first described by Cushing[32] and attributed by him to basophilic adenoma of the pituitary gland It has since been known as the *Cushing syndrome* Subsequently, the symptom-complex was found by other workers in association with tumors of other endocrine glands and basophilic adenomas are often found to be unassociated with the syndrome

Clinical Manifestations

In the majority of cases, hypertension may exist for a number of years without any disturbing symptoms until the patient's attention is called to it by the physician Soon after, some patients begin to suffer from *imaginary or actual disturbances, resulting mainly from fear* Also, many cases suffering from unrelated conditions will attribute all their symptoms to their "high blood pressure"

On the other hand, a great many other cases do suffer from various disturbances that may be traceable to the hypertension itself, such as intermittent or continuous headaches, fullness in the head, dizziness, disturbances in vision, ringing in the ears, the anginal syndrome in various degrees, and others The headaches are usually occipital, and in severe cases are excruciating The various symptoms usually occur in cases where the blood pressure is very high and persistent, although some cases with mild grades of hypertension may also experience them from time to time when a temporary rise occurs. In nearly all cases there may be a spontaneous remission of symptoms for variable periods of weeks or months and exacerbation at other times

The serious effects of hypertension lie in its predisposition to arterio- and arteriolar sclerosis, resulting in acute or chronic cerebral, cardiac and renal debilitating and fatal disease This usually develops earlier in the higher grades of hypertension than in the milder ones. We see, however, many cases of low-grade intermittent hypertension with marked arteriosclerosis affecting various structures or organs. In fact, we often observe marked arteriosclerosis *without hypertension*

The clinical manifestations of hypertension, when arteriosclerotic degenerative changes develop vary greatly with the extent of the arteriosclerosis and with the organ or organs which are predominantly involved Some of the manifestations are described in Chapter XIX. Because the heart is the most frequent organ affected, and because the hypertension itself, even in the absence of coronary sclerosis, may produce a cardiac breakdown, hypertensive heart disease will be more fully described shortly.

Prognosis

There are many factors which determine the prognosis of hypertension, some of which are not ascertainable. The most important are the age of onset of hypertension, the rapidity of its progress, the underlying causes, and the rapidity of the development of arteriolar sclerosis.

Individuals who develop hypertension early in life may succumb to cardiac, renal or cerebral complications by the time they reach middle life Those who develop the condition at about middle life or later may reach or even surpass the average normal span of life. In this respect it resembles diabetes mellitus In juvenile diabetes there is a shorter longevity and the cardiovascular complications develop earlier than in individuals who develop the condition later in life. In both juvenile diabetes and juvenile essential hypertension the hereditary factor appears to play the greatest role in their etiology, and this factor can not be changed by therapy. Of course, the retardation of the progress of the given disease is possible by proper therapeutic procedures

The rapidity of progress of hypertension varies markedly in different individuals In some it progresses extremely slowly over many years The author has on record many cases with hypertension of twenty to thirty years' duration with practically no discomfort, when the fear element is eradicated from their minds On the other hand, many other cases show a rapid progressive increase in blood pressure over a period of a few years with early development of arteriosclerosis and severe complications, reaching the stage of so-called "malignant hypertension" within a comparatively short period In some of these cases a pregnancy or a severe infec- [illegible]

corrected

In essential hypertension, the rapidity of onset of arteriolar sclerosis is the most important determining factor of the prognosis in the given case. This may be ascertained from the rapidity of onset of cerebral, renal, cardiac or retinal changes In this respect a persistently high diastolic blood pressure is more indicative of widespread arteriolar changes than a high systolic or a high diastolic pressure with a frequent intermittent drop The latter condition speaks for a considerable degree of arteriolar spasm besides structural vascular changes as the underlying cause.

The prognosis is serious in any case where the diastolic pressure is persistently 130 mm. of Hg or over and where no spontaneous drop occurs

or no temporary drop is induced by the use of nitrites. At this stage it must be assumed that the structural arteriolar changes are far advanced and are mainly responsible for the hypertension. The degree of a spontaneous drop in the diastolic pressure, or a temporary drop induced by nitrites, if present, may be taken as an index of the part the functional element plays in the maintenance of the hypertension in the given case.

The causes of death in hypertension vary somewhat in the different reported series of cases The Bell and Clawson[33] series may, perhaps, be taken as the average In a postmortem study of 410 cases of essential hypertension they found that in 44 5 per cent death was due to congestive heart failure, in 19 per cent to cerebral hemorrhage or thrombosis, in 16 per cent to coronary disease, in 8 5 per cent to renal insufficiency and in 12 per cent to other conditions

Treatment

Before attempting to discuss the treatment of hypertension, the author considers it pertinent to quote the following from Weiss and English,[34] which aptly describes the fads and fancies generally employed in therapy

"Let us take again the example of a middle-aged man refused by a life insurance company because of high blood pressure His physician rules out glomerulonephritis and decides that the patient is suffering from essential hypertension Then, all too frequently, attention is concentrated on the effort to 'bring the blood pressure down ' The patient demands to know the blood pressure figure, on each visit to the physician he waits with anxious concern to hear the latest reading and frequently he has ideas of 'stroke,' 'heart failure' or 'Bright's disease' in the back of his mind

"Just what has been done to this poor patient in the effort to 'bring his blood pressure down'? Because of an ill-founded idea that protein is responsible for hypertension and kidney disease he is denied meat and eggs, especially red meat, which for some reason is looked upon with particular dread Then his diet is rendered even more unpalatable by the withdrawal of salt One would sympathize with this half-starved victim of good intentions except that he probably would not be able to eat anyway, his teeth having been removed on the theory that focal infection has something to do with hypertension Even before this period he has sacrificed his tonsils and has had his sinuses punctured because of the same theory. In case he actually had been able to eat some solid food, in spite of these previous therapeutic measures, the slight colonic residue was promptly washed out by numerous 'colonic irrigations,' especially during the period when the theory of autointoxication was enjoying a wave of popularity. To add to his unhappiness *he may be told to stop work and exercise, and* of course is denied alcohol and tobacco as well as coffee and tea. And now to cap the climax of his difficulties, the unfortunate person with hyper-

tension has been referred to the neurosurgeon, who is prepared to separate him from his sympathetic nervous system."

This summary adds a bit of humor to a pathetic state, but has, however, a considerable amount of truth.

In view of the lack of a complete knowledge of the pathogenesis of essential hypertension, all therapy employed must necessarily be empiric. We can not treat any abnormal state with scientific exactness if we do not know its abnormal underlying causes. Nevertheless, the facts we do know *about essential hypertension are sufficient to map out a logical routine of* therapy consistent with such knowledge.

The facts are that spasticity of the arterioles induces the arterial hypertension The hypertension is therefore an attempt on the part of nature to overcome the peripheral resistance It is, in a sense, compensatory We also know that arteriolar spasticity induces a greater or less degree of tissue anoxia, leading eventually to molecular tissue destruction. When vital organs such as the heart, brain or kidneys are affected, functional insufficiency of those organs gradually develops, resulting in the clinical manifestations of the disease, also, myocardial insufficiency may result from the high arterial pressure

The main therapeutic indication, therefore, is to attempt to reduce arteriolar spasticity by methods which do not suddenly and unduly produce a marked fall in blood pressure. The latter condition is important, especially, in the later stages of the hypertensive state when structural arteriolar changes have progressed to a high degree Sudden lowering of pressure under such circumstances will produce greater impoverishment of the blood supply to the tissues which may result in severe acute destructive changes of the organs mostly involved.

Here, the author wishes to express his unequivocal feeling, based on a considerable experience, that drug therapy of any kind has no logical place in the management of hypertension He fully agrees with the findings of Ruskin and McKinley[35] that the best symptomatic relief is obtained from a placebo Such drugs as the nitrites, thiocyanates, and the xanthines either have no effect, or produce an abrupt temporary fall in pressure which

although for temporary relief, at times, the barbiturates are also of value *The advantage of the bromides is that they may be used for a long period,* if necessary, without developing a tolerance. This is not true of the barbiturates which become less effectual as time goes on Inasmuch as a very small proportion of cases may develop bromide intoxication, we must watch out for signs of such effects

In the proper management of a hypertensive case, even the sedatives

are to be employed only during periods when acute symptoms occur. The main therapeutic approach should be from a viewpoint of eliminating all intrinsic and extrinsic bodily factors which are likely to produce arteriolar spasm This implies a thorough study of the individual case, especially with reference to his mental state, the presence of infection, his work, his play, rest, and diet, all of which must be corrected where necessary.

The Mental State It is a common observation that in most cases of hypertension, especially in the early stages, the complaints of the patient are not related to the height of blood pressure They have, at times, marked disturbances when their blood pressure is low, and may be free from symptoms when the blood pressure is high This would indicate that subjectively the symptoms are not always directly dependent on the increase in blood pressure In many cases they are neurogenic in origin, due to fear of the hypertensive state. In many others they are due, undoubtedly, to the same factors which raise the blood pressure In still others, they may be due to tissue anoxia in different parts of the body from time to time due to arteriolar spasticity It is of prime importance, therefore, that the patient be reassured. He must be told that the elevation in his blood pressure is of no importance and that his symptoms are not related to it Everything should be done to remove his blood pressure consciousness He is to be told that the blood pressure rise is merely a symptom, not a disease, and that it will diminish under proper mental relaxation and the avoidance of worry. Even if it does not diminish it has no serious immediate effects, and many persons live with high blood pressure longer *than with normal or subnormal pressure* *He must be made to understand* that it is of no importance or value to bring down the blood pressure In fact, the rise in blood pressure may be very essential to maintain normal circulation in his case

Psychopathologic investigations by various workers appear to have demonstrated that inner mental tension, repressed aggressions and anxieties which may be hidden, to a great extent, by higher consciousness and self control may find expressions in various somatic disturbances, as described in Chapter XXIX Hypertension is probably one of those bodily expressions of occult psychic tension. If such is the case, prolonged arteriolar spasm, which is the cause of persistent hypertension, may at least partly, *be due to subconscious disturbances* That visible emotional disturbances temporarily increase the blood pressure is well established It is very likely, *therefore, that subconscious disturbances have a more prolonged* angiospastic effect.

In the therapy of hypertension, it is important, therefore, to study the mental makeup of the individual in an attempt to uncover, if possible, any hidden emotional strain and conflict. Making the patient aware of

the condition may help much in lowering the blood pressure and the symptomatology.

Removal of Infections: The theory of chronic focal infection as a cause of hypertension has lost its popularity in recent years, and for good reason. Promiscuous surgery may be greatly disturbing if not detrimental to the patient. However, the removal of a unilaterally infected kidney will often relieve a hypertensive state. The removal of a chronically infected gall bladder with acute exacerbations may help the general condition of the patient, and relieve reflex cardiac disturbances, but usually no change in blood pressure occurs. The same is true of other evident infections.

[illegible]

rest must be strictly prohibited Most of these patients are too tense and serious in their work habits and they must be taught not to be overconscientious. It is most important for many of them to learn not to be too aggressive, and to look at life from a more philosophic viewpoint

Advice as to Rest and Recreation: All hypertensive patients require more rest than normotensive individuals This is due to the fact that the metabolic rate is increased in hypertension, as was recently shown by Rosenkrantz and Marshall.[36] The amount of rest required is to be measured by the amount of work the patient does, by the degree of hypertension and by the presence or absence of complicating factors.

In the early phases, eight to ten hours of bed rest and sleep are essential daily In addition, the patient is to learn to rest and relax for a half hour before and after each meal, and whenever possible Acquiring the habit of relaxation is a difficult task for any one, especially for the hypertensive individual Prolonged practice by the patient, properly guided by the physician is necessary to get good results

It is not within the scope of this book to describe the art of relaxation. The subject is well covered by Jacobson[37] Suffice it to say that the patient must learn to become conscious of his muscular and nervous tension, and must attempt to overcome it by gradual relaxation If properly carried out after prolonged practice it may prove to be the most important therapeutic measure we have.

At this stage, it is wise for the patient to take at least a day off once a week for some open air activity Long walks, golfing, fishing, and other similar activities are very essential, and help to divert the patient's mind from his daily business or occupational worries.

In the later stages of the hypertensive state, more rest and relaxation are called for, and much of his work will have to be curtailed. The extent of curtailment depends upon the functional capacity of his heart and

peripheral circulation This must be carefully determined in each individual case No blanket rule can be layed down for all cases At this stage it is also wise to have the patient rest one day a week in bed, and the number of hours of daily rest is to be increased. Of course, when cardiac or renal failure ensues, prolonged rest is necessary, as described in Chapter XIII

Advice as to Diet A great deal has been written in the past on the treatment of hypertension by specific diets and the pendulum has swung in one direction or the other as to the amount of salt and nitrogenous materials to be used

In the early stages of hypertension the dietary problem is of no importance There is only one restriction necessary, namely not to eat more than is required to maintain normal health and strength, and to carry on normal activities The diet should be well balanced with a sufficient amount of nitrogenous materials to take care of wear and tear of body tissues Perhaps, the equivalent of 50 to 70 grams of nitrogen per day in individuals of various weights should be sufficient The salt intake, likewise, should be enough to make the food palatable, but should not be used much in excess of that

There is one essential requirement in the dietotherapy of these cases—the reduction of weight where necessary. This is a most important therapeutic measure The food intake must be greatly limited in all cases who present a higher weight than the average for the given height and age of the individual The amount of food reduction is dependent upon the degree of overweight Reduction in weight should, however, be carried out slowly

The effects of the diminution of food intake on cardiovascular dynamics were well demonstrated in a recent study by Brozek and co-workers.[35] They made laboratory investigations of many individuals on the effect of a starvation diet on the dynamics of the circulation They have also analyzed the effect of starvation in large portions of the European populations, especially in Leningrad, Russia during World War II

In most cases, both normotensive and hypertensive, there was a lowering of the blood pressure during the starvation period It is also important to observe from their study that during recovery from starvation, the [illegible]

The mechanism of those manifestations can be readily understood when we realize that ordinarily the metabolic rate of the body is in direct proportion to the food intake and the cardiovascular dynamics is greatly influenced by the metabolic activities. Sudden increase in such activities by increasing the food intake after starvation finds the cardiovascular system unprepared to cope with the increased metabolism.

In the later phases of hypertension when considerable renal or cardiac insufficiency has developed, dietary restrictions must be more rigid This applies particularly to the sodium chloride and nitrogen intake. At this phase the rice diet devised by Kempner[39] may, perhaps, be found to be of value. This diet consists essentially of rice, fruit juices and sugar, to which are added the vitamins and iron. The daily caloric intake varies with the weight of the patient If normal, he allows 2,000 calories per day, made up predominantly of carbohydrates which he recommends in the amount of 460 to 470 grams per day. The total protein intake is 15 to 25 grams, sodium 0 25 to 0 4 grams, and fat 5 grams.

It is very likely that the value of this diet is due to the extremely low sodium content, which is the best therapy in congestive heart failure, as shown in Chapter XIII, and which is of great help in renal insufficiency. A less rigid diet with similar restriction in the sodium chloride intake will probably prove to be as efficient

The fluid intake in hypertension need not be restricted at any stage, as described in Chapter XIII.

Advice as to Sympathectomy The successful results of sympathectomy in the treatment of hypertension reported within recent years by various surgeons resulted in a wave of enthusiasm among doctors and patients alike. From personal observations of a few patients who underwent the various operations, the author was not quite convinced of its therapeutic value. That it gave relief in some cases was true, but the relief was not universal. Furthermore, some cases had symptomatic relief even when the blood pressure returned to a high level Others had no relief even when the blood pressure was reduced.

Fishberg[40] recently reported the results of a follow-up of 119 cases of severe hypertension for variable periods after sympathectomy. He concluded that the operation is indicated in less than 4 per cent of cases with hypertension He feels that operation may be advisable only in those cases which do not respond to rigid rest and sodium chloride restriction. It is also indicated in cases which show a rapid downhill course with a sudden development of a persistently high diastolic pressure of 130 mm. or over, papilledema, retinal hemorrhages or exudates, intractable headaches, hypertensive encephalopathy or cerebral hemorrhage, and heart failure which responds to treatment. He believes that the presence of impairment of renal function, irreducible congestive heart failure, and coronary or *cerebral arteriosclerosis are contraindications to this operation*

HYPERTENSIVE HEART DISEASE

Hypertension is one of the most important causes of heart disease. It is usually associated with coronary sclerosis, in which case, the cardiac disturbances may be due primarily to the latter, although the hypertensive element may be an important additional factor. In many hypertensive

cases, however, the cardiac manifestations are due primarily, or only, to the hypertension, the degree of coronary disease, if any is present, being insufficient to produce the cardiac changes.

Pathology

The primary cardio-aortic changes in hypertension are left ventricular hypertrophy and aortic dilatation with atherosclerotic changes. The left

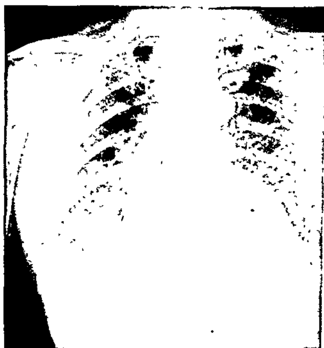


FIG 85 —FROM A FEMALE, 48 YEARS OLD WITH ADVANCED HYPERTENSIVE CARDIOVASCULAR DISEASE Marked tortuosity and dilatation of the aorta, shown by a greatly accentuated and broad knob, and marked bulge of the ascending portion The left ventricle is also greatly enlarged

ventricular hypertrophy is due to greater strain thrown on the left ventricle by the increased intra-arterial pressure. The aortic dilatation is due to greater distention of the aorta caused by the increased peripheral resistance. Both the cardiac hypertrophy and aortic dilatation vary in degree with the height of the blood pressure and with its duration. The author's experience has been that in many cases, before cardiac failure occurs, there appears to be a reciprocal relationship of aortic dilatation and cardiac hypertrophy. Those cases which present a greater degree of aortic dilatation usually show a relatively lesser degree of demonstrable cardiac hyper-

trophy and vice versa These are shown in Figures 43 and 44. In advanced cases, both the aorta and the left ventricle are affected, as shown in Figure 85.

Where the aorta is greatly dilated, its immediate branches may also show a variable degree of dilatation.

Left ventricular hypertrophy, in the early stage, is concentric and may not be detectable either clinically or roentgenologically This stage may



FIG 86—FROM A MALE, 56 YEARS OLD, WITH MARKED HYPERTENSION The aorta is tortuous and markedly knobbed, and there is some left ventricular enlargement

last, in some cases, many years As time goes on, however, the hypertrophy becomes more marked. When failure occurs, dilatation of the left ventricle develops which suddenly and progressively increases the size of the heart. *These are illustrated in Figures 86 and 87.*

In occasional cases, left ventricular hypertrophy involves the interventricular septum in a marked degree, greatly exaggerating its natural bulge into the right ventricle. In some of these cases, in the course of left ventricular dilatation, the bulge of the interventricular septum into the right ventricle may be so marked as closely to approach the right wall

and interfere with the normal flow of blood through the right heart. This results in signs simulating right heart failure The condition was first described by Bernheim,[41] and the resulting symptom-complex has since been known as Bernheim's syndrome.

Cardiac hypertrophy in hypertension, as in other forms of ventricular muscle hypertrophy, is due to increased width of the muscle fibers This



FIG 87—SAME CASE AS IN FIG 86, THREE AND ONE-HALF YEARS LATER, WITH THE DEVELOPMENT OF LEFT HEART FAILURE The aortic widening is more diffuse, and the heart enlargement is much more marked There is also an increase in the hilar markings, and there is a slight amount of fluid in the right chest cavity

results in a relative diminution of the capillary blood supply per unit of muscle tissue, as described in Chapter VI Relative ischemia of the heart muscle tissue is the underlying cause of the clinical manifestations of the disease. In uncomplicated hypertensive heart disease, therefore, the gross appearance of the left ventricle at autopsy is thick and rather pale and no degeneration or inflammation is found microscopically. In many cases,

there are the additional factors of coronary sclerosis and occlusive processes which modify the appearance of the heart muscle at autopsy

Clinical Manifestations

As said before, hypertension may exist in some cases for many years without cardiac disturbances If the patient does not succumb to other complications, however, symptoms and signs of cardiac involvement will sooner or later supervene.

Symptoms: The early symptoms may be palpitation, precordial pain, oppression or discomfort and some degree of dyspnea. These, however, are often dwarfed by symptoms referred to other systems of the body, particularly the central nervous system

Palpitation usually occurs on excitement or exertion but it may, at times, appear spontaneously. In the latter case, it is often due to transient arrhythmias or tachycardias, as in other conditions.

Precordial pain occurring in hypertensive heart disease is usually dull, prolonged and of an ill-defined nature In some cases, there is a sense of oppression or other discomfort, instead of pain. The underlying cause may, perhaps, be the relative myocardial ischemia which becomes more marked under conditions of strain or excitement In most cases, however, it appears to be of neurogenic or reflex origin If the pain assumes the characteristics of the anginal syndrome, it is usually caused by an associated coronary sclerosis. The characteristic attacks of coronary occlusion that occur in hypertensive heart disease are the same as in nonhypertensive cases.

Dyspnea is a much more frequent symptom of hypertensive heart disease than is pain In the early stages, it occurs only after more or less exertion As the disease progresses, dyspnea becomes more pronounced and may soon begin to occur spontaneously, while at rest, awaking the patient at times from sleep in the middle of the night, a condition spoken of as paroxysmal nocturnal dyspnea, and is frequently associated with pulmonary edema, as described in Chapter XIII. It is interesting to note that whereas in arteriosclerotic heart disease without pre-existing or coexisting hypertension, severe angina pectoris and repeated coronary occlusion may occur without nocturnal dyspnea and pulmonary edema, in hypertensive heart disease, the latter are the outstanding manifestations In the absence of gross coronary sclerosis in hypertensive heart disease, severe dyspnea and pulmonary edema may be the only manifestations, pain being either entirely absent or insignificant

Physical Signs In the early phases and when hypertension is not marked, there may be no abnormalities of the heart. We often see patients with hypertension of many years' duration with no demonstrable cardiac enlargement, and only minimal aortic dilatation and tortuosity. In many

such cases, concentric hypertrophy occurs which cannot be determined by examination. It may be demonstrated in some of these cases by left ventricular preponderance in the electrocardiogram In many cases, however, especially when the blood pressure is high, more or less cardiac enlargement and aortic changes gradually become demonstrable by physical and roentgenologic findings.

Of greater importance than cardiac enlargement is the character of the heart sounds. From the early stages of the disease till the period when definite left heart failure occurs, the first heart sound at the apex and the second sound at the aortic area are accentuated. The latter often assumes a ringing quality The degree of accentuation is in direct proportion to the height of the blood pressure As time goes on, a systolic murmur gradually develops at the aortic area due to aortic dilatation

When left heart failure supervenes, cardiac enlargement becomes a prominent finding, and increases in proportion to the degree of failure. The heart sounds, on the other hand, gradually lose their accentuated quality and become weaker. The degree of diminution in their quality, likewise, corresponds to the degree of failure. In addition to the aortic systolic murmur, a similar murmur may soon develop at the apex due to functional mitral incompetency, as described in Chapters IX and XXIV In an occasional case, a short aortic diastolic murmur may also develop due to sclerotic changes of the aortic leaflets Later, a gallop rhythm develops and the pulmonic second sound becomes accentuated. Pulsus alternans may occur The extracardiac signs of left heart failure, such as pulmonary stasis and edema become marked, as described in Chapter XIII. The various arrhythmias may occur at any time

We often find considerable expansile pulsation above the manubrium, close to the inner end of the right clavicle in marked hypertension. This is more apt to occur in obese individuals with high diaphragms

In the comparatively rare cases of the Bernheim syndrome, the outstanding signs are those that occur in right heart failure such as venous stasis, liver enlargement, peripheral edema, and so on There is, however, the absence of any condition such as mitral stenosis or pulmonary disease that would bring about right heart failure There is also no evidence of demonstrable left heart failure, which in the late stages is followed by right heart failure, as described in Chapter XIII The condition should be suspected where isolated right heart failure occurs in hypertensive heart disease in the absence of definite dyspnea and pulmonary stasis.

One of the author's patients, a woman, fifty-six years of age, presented [illegible]

to 140 diastolic. Although her heart was markedly enlarged, the lungs

endurance of a more strenuous life, and seek an easier type of work On the other hand, a sedentary occupation may be the underlying cause of low blood pressure, in many cases

In normal individuals with higher blood pressure readings, a temporary drop to the low figures may occur during sleep and after great relaxation

The *pathologic conditions* that may be associated with very low blood pressure are numerous They may be divided into acute, subacute, and chronic forms

The acute forms are observed in shock due to any cause, in acute infectious diseases, acute intoxications, sunstroke, after extreme physical and nervous exhaustion, and in cases of massive pericardial effusion. An interesting, but rare form of acute hypotension is the so-called "postural hypotension" described by Bradbury and Eggleston[44] or "orthostatic hypotension" by MacLean and Allen[45] In this condition the patient may present normal blood pressure in the sitting or reclining positions, but an extreme drop in pressure occurs when he assumes the upright posture Associated with this drop in pressure there is marked weakness, dizziness, slight acceleration of the heart rate and sweating At times syncope may occur The condition is aggravated in hot weather

The subacute or chronic forms of hypotension may occur in nutritional diseases, anemias, cachexias, certain chronic infections such as tuberculosis, and in Addison's disease.

Clinical Manifestations In most individuals, low blood pressure is asymptomatic. They may carry on their accustomed daily activities without discomfort or complaints If called upon to do unusually strenuous work however, they will present evidence of circulatory insufficiency

Some hypotensive individuals, however, may show, from time to time, signs of fatigue and lack of energy and experience dizziness, syncope, nervousness, insomnia, poor power of concentration, and sensory disturbances Others may experience precordial oppression or actual pain coming on after exertion which may be indistinguishable from mild angina pectoris, and may tax the ingenuity of the physician to exclude the presence of coronary disease. Some also complain of palpitation and digestive disturbances.

The symptoms are, in most cases, intermittent with periods of well being in between During the symptomatic period the blood pressure is usually found to be lowest

In those cases where the low blood pressure occurs as a result of the various pathologic states mentioned before, the clinical manifestations are those of the primary underlying disease. The hypotension here is merely *one of the manifestations* of the given disease, although it may be a contributing cause of many of the symptoms.

Prognosis: Low blood pressure in individuals who otherwise have no demonstrable organic disease does not shorten life. In fact, according to life insurance statistics, the life expectancy of persons with low blood pressure is longer than usual. This is due to the fact that an individual with this condition usually knows his limitations, and does not overstrain himself. Furthermore, low blood pressure throws less of a strain on the cardiovascular system than normal blood pressure, and far less than hypertension

When the hypotension is due to the various diseased states mentioned before, the prognosis is governed by the underlying disease in the given case.

Treatment Hypotensive individuals with no organic disease require no drug therapy. Their general health should be maintained by proper nutrition, the vitamins, open air life and activity consistent with comfort. Cool showers taken daily, ocean bathing and massaging all help to stimulate the vasomotor system and body musculature.

In those cases where low blood pressure is due to diseased states, treatment should be directed to the underlying disease

REFERENCES

1 Holman, D V, and Page, I H The cardiac output in arterial hypertension Am Heart J 16 321, 1938
2 Austrian, C R The viscocity of blood in health and disease Bull Johns Hopkins Hosp, 22 9, 1911
3 Linder, K, Lundsdgaard, C, and Van Slyke, D D Changes in the volume of plasma and the absolute amount of plasma proteins J. Exper Med 29 921, 1928
4 Wiggers, C J The dynamics of hypertension Am Heart J 16 515, 1938
5 Tigerstedt, R, and Bergman, P G Niere und Kreislauf Skand Arch f Physiol 8 223, 1898
6 Fishback, H R, Dutra, F E, and MacCamy, E T The production of chronic hypertension in dogs by progressive ligation of arteries supplying the head J Lab & Clin Med 28 1187, 1943
7 Gregory, R, and Levin, W C Studies in hypertension The effect of high spinal anesthesia on the blood pressure of patients with hypertension and far advanced renal disease Its possible relationship to the pathogenesis of hypertension J Lab. & Clin Med 30 1037, 1945
8 Goldblatt, H, Lynch, J, Hanzel, R F, and Summerville, W W Studies on experimental hypertension I The production of persistent elevation of systolic blood pressure by means of renal ischemia J Exper. Med 59 347, 1934
9 Corcoran, A C, and Page, I H Observations on the relation of experimental hypertension to renal clearance and renal ischemia Am J Physiol 123 43, 1938
10 Goldblatt, H Experimental Hypertension Induced by Renal Ischemia Harvey Lectures Baltimore, Williams & Wilkins, 1937-1938
11 —— Studies on experimental hypertension. Pathogenesis of experimental hypertension due to renal ischemia Ann Int Med 11 69, 1937
12 Page, I H The effect of bilateral adrenalectomy on arterial blood pressure of dogs with experimental hypertension Am J Phys 122 352, 1938.
13 Glenn, F, Child, C G, and Page, I H. The effect of destruction of the spinal cord on hypertension artificially produced in dogs Am. J Physiol 122 506, 1938

[14] Kohlstaedt, K G, Helmer, O M, and Page, I H Activation of renin by blood colloids Proc Soc Exper Biol & Med 39 214, 1938
[15] Braun-Menendez, E., Fasciolo, J C, Leloir, L. F, and Munoz, J. M The substance causing renal hypertension J Physiol 98 283, 1940.
[16] Page, I H, and Helmer, O M A crystalline pressor substance, angiotonin, resulting from the reaction between renin and renin-activator. J Exper Med 71 29, 1940
[17] ——: Studies on the mechanism of arterial hypertension J A M A 120 757, 1942
[18] ——, Helmer, O M, Kohlstaedt, K G, Kempf, G F, Gambill, W D., and Taylor, R D The blood pressure reducing property of extracts of kidney in hypertensive patients and animals Ann Int Med 15 347, 1941
[19] ——, ——, ——, ——, Corcoran, A C, and Taylor, R D A progress report of investigations concerned with the experimental treatment of hypertension with kidney extracts Ann Int Med 18 29, 1943
[20] Goldblatt, H, Kahn, J R, and Lewis, H A Studies on experimental hypertension XVII Experimental observations on the treatment of hypertension J.A M A 119 1192, 1942
[21] Ayman, D Heredity in arteriolar hypertension Arch Int Med 53 792, 1934
[22] Hines, F A Hereditary factor in essential hypertension Ann Int Med 11 593, 1937
[23] Schulze, V E, and Schwab, E H Arteriolar hypertension in the American Negro Am Heart J 11 66, 1936
[24] Moschcowitz, E The causes of hypertension of the greater circulation J A M A 93 347, 1929
[25] Ayman, D The personality type of patients with arteriolar essential hypertension Am J M Sc 186 213, 1933
[26] Briger, L, Ackerman, N W, Cohn, A E Schroeder, H A, and Steele, J M Personality in Arterial Hypertension New York, Am Soc for Research in Psychosomatic Problems, 1945
[27] Smith, H W, Goldring, W, and Chasis, H The measurement of the tubular excretory mass, effective blood flow and filtration rate in the normal human kidney J Clin Investigation 17 263, 1938
[28] Sigler, L H Spontaneous non-rhythmic variations in the blood pressure levels and in the "silent gap" Am J M Sc 177 494, 1929
[29] Levy, R L, Hillman, C C, Stroud, W D, and White, P D Transient hypertension Its significance in terms of later development of sustained hypertension and cardiovascular renal disease J A M A 126 829, 1944.
[30] Sigler, L H Periodic variability of some forms of arterial hypertension Am J M Sc 172 543, 1926
[31] Oppenheimer, B S, and Fishberg, A M Association of hypertension with suprarenal tumor Arch Int Med 43 631, 1924
[32] Cushing, H · The basophil adenomas of the pituitary body and their clinical manifestations (pituitary basophilism) Bull Johns Hopkins Hosp 50 137, 1932
[33] Bell, E T, and Clawson, B J Primary (essential) hypertension Arch Path 5 939, 1928
[34] *Weiss, E, and English, O S Psychosomatic Medicine* Philadelphia, W B Saunders Co, 1943 Pages 118–119
[35] Ruskin, A, and McKinley, W F Comparative study of potassium thiocyanote and other drugs in the treatment of essential hypertension Am Heart J 34 691, 1947.
[36] Rosenkrantz, J A., and Marshall, C · Basal metabolic rate in hypertensive vascular disease Arch Int Med 80 81, 1947
[37] Jacobson, F: Progressive Relaxation Chicago, University of Chicago Press, 1929

[38] Brozek, J, Chapman, C B, and Keys, A · Drastic food restriction Effect of cardiovascular dynamics in normotensive and hypertensive conditions J.A M.A. 137 1569, 1948.
[39] Kempner, W.. Treatment of kidney disease and hypertensive vascular disease with rice diet North Carolina M J 5 125, 1944, ibid 5·273, 1944; Compensation of renal metabolic dysfunction North Carolina M J. 6 61, 1945
[40] Fishberg, A M Sympathectomy for essential hypertension J.A M A 137 671, 1948
[41] Bernheim Venous asystole in hypertrophy of the left heart with associated stenosis of the right ventricle Rev. de Med 30·785, 1910
[42] Russek, H I, and Zohman, B L.: The syndrome of Bernheim Am Heart J. 30 427, 1945
[43] Barach, J H: Arterial hypotension Arch Int Med 35 151, 1925.
[44] Bradbury, S, and Eggleston, C "Postural hypotension" Am Heart J 1 73, 1925
[45] MacLean, A R, and Allen, E V. Orthostatic hypotension and orthostatic tachycardia J A M A 115 2162, 1940

CHAPTER XVIII

Pulmonary Vascular Hypertension and Cor Pulmonale

Although we have no direct way of measuring the pulmonary arterial blood pressure in the living human and we therefore do not know to what extent pulmonary arterial hypertension exists, we may assume that it does exist to a great extent from the accentuated pulmonic second sound, dilatation of the pulmonary artery and right ventricular hypertrophy that occur in cases where there is interference with the free flow of blood through the pulmonary vascular tree.

Unlike systemic essential hypertension which is due to widespread *functional* arteriolar constriction, whatever the cause may be, intrapulmonic arterial hypertension is probably caused predominantly or only by *structural* interference with the free flow of blood through the pulmonary vascular tree It is doubtful if there is any such condition as essential pulmonary arterial hypertension. It certainly does not coexist with systemic arterial hypertension This is evidenced by the fact that in systemic hypertension, no matter how advanced, there is no evidence of embarrassment of the right ventricle The right ventricle in such cases becomes embarrassed only when left heart failure ensues with the resulting increased stasis in the pulmonary circulation Conversely, right ventricular hypertrophy and failure may occur in any structural disease which mechanically interferes with the free propulsion of blood through the pulmonary vascular tree whether or not systemic hypertension is present In an extensive review of the literature, Brenner[1] found that although experimental evidence is conflicting, it appears to be generally accepted that the vasomotor influence on the pulmonary vessels is feeble and is of little importance in regulating the flow of blood through the lungs

Underlying Pathology· There are many pathologic states of the heart, lungs and pulmonary vessels which increase the resistance to the free flow of blood through the pulmonary arteries resulting in pulmonary arterial hypertension and right ventricular embarrassment

The most important forms of *heart disease* producing this condition are mitral stenosis and certain congenital defects, discussed in Chapters XXIV and XXVII

Of the various *lung diseases* that may produce pulmonary arterial hypertension are primary diffuse emphysema, bronchial asthma, chronic bronchitis and massive bronchiectasis, diffuse pulmonary fibrosis and pulmonary

tuberculosis. It appears from the various reports in the literature, however, that nearly all pulmonary disease that gives rise to intrapulmonic arterial hypertension has an associated emphysema. n other words, it is probably the emphysema, either primary or secondary, which predisposes to this condition. Spain and Handler[2] suggest that the distention and increased pressure in the alveoli produce compression of the arteriolo-capillary tree, thus interfering with the free flow of blood through these channels which results in increased pressure in the pulmonary arteries This mechanism was also considered many years before by Cloetta[3] who suggested that destruction of part of the capillary bed in the lungs due to intra-alveolar pressure was probably an additional factor.

In rare cases of marked *chest deformity*, pulmonary vascular hypertension may occur. Here, it may also be due mainly to associated pulmonary pathology Spain and Handler feel that kinking of the great pulmonary vessels might be another cause in such cases. This is also considered one of the possible mechanisms by Fishberg [4]

Of the *pulmonary vascular diseases* that may conceivably produce intrapulmonic arterial hypertension, there are acute, subacute and chronic conditions *Pulmonary embolization* from thrombophlebitis in any part of the body or from mural thrombi in the right heart chambers may produce the acute form of pulmonary arterial hypertension, if the embolic occlusion of the pulmonary vessels is extensive enough The subacute form may occur in carcinomatous metastasis to the lung with infiltration of the perivascular lymphatics and secondary involvement of the pulmonary arterioles, as described by Greenspan [5]

The chronic form of intrapulmonic arterial hypertension may occur in *infectious arteritis* and in rare conditions of *thromboangitis obliterans* as well as *endarteritis obliterans* of the pulmonary arterioles Thompson and Gerstl[6] report a case of thromboangitis obliterans of the pulmonary vessels with aneurysm of the pulmonary artery Endarteritis obliterans has recently been discussed by Bedford and co-workers[7] in connection with bilharzial disease. It may also occur in *syphilitic and tubercular vascular involvement* Of course, *pressure on the pulmonary artery* or one of its main branches by an aortic aneurysm may also produce intrapulmonic arterial hypertension

Primary arteriosclerosis and dilatation of the pulmonary vessels is very rare Under the title "Idiopathic Dilatation of the Pulmonary Artery," Oppenheimer[8] reported eight cases and found only one previously reported case in the literature. He considered [illegible]

[illegible]

findings. Gold[9] reported another case. The majority of cases of pulmonary arteriosclerosis and dilatation are secondary to the pathologic changes enumerated above. This applies also to so-called Ayerza's disease which is supposed to be a condition of primary arteriosclerosis of the pulmonary artery, originally thought by the author to be due to syphilis and the etiology of which has later been refuted. Moschcowitz[10] feels that the name Ayerza's disease should be abandoned

Cor Pulmonale

Intrapulmonic arterial hypertension, whether caused by cardiac, pulmonary parenchymal or pulmonary vascular disease, if prolonged and progressive, may result sooner or later in overburdening and failure of the right ventricle. If the term "cor pulmonale" is used to designate such a condition, it should properly be applied to all such cases, regardless of the underlying pathology that produces right ventricular strain. However, inasmuch as mitral stenosis and congenital heart disease are distinct clinical entities, the term "cor pulmonale" is being reserved for right ventricular hypertrophy and failure due to pulmonary parenchymal and vascular disease

As said before, the condition may be acute, subacute and chronic.

Acute Cor Pulmonale: This is characterized by a sudden dilatation of the pulmonary artery and right heart caused by acute massive pulmonary embolization If severe enough, sudden right heart failure ensues.

The *underlying causes* are venous thrombosis anywhere in the body or mural thrombi in the right ventricle which serve as emboli. These are discussed in Chapter XIX.

Pulmonary embolization occurs quite frequently In a review of 1,000 consecutive autopsies, not including bacterial endocarditis and traumatic injuries, Spain and Moses[11] found the incidence of pulmonary embolization to be 10 9 per cent The frequency of venous thrombosis as a source of embolization, in their experience, was twice as great as that of mural thrombi in the heart Allen and co-workers,[12] however, cited Castleman who found that 95 per cent of pulmonary embolization is derived from venous thrombosis of the deep leg veins. They also cite Davis who found an incidence of pulmonary embolization in 3 out of every 1,000 postoperative cases According to Morton and co-workers,[13] the greatest frequency of fatal embolization occurs in patients over 50 years of age. There is no sex difference.

The detachment of mural thrombi in the venous system, according to Chapman and Linton,[14] may in some cases be caused by sudden transient distention of the systemic veins. This may occur in the acts of defecation, parturition, coition, lifting and straining at work which produce the effect of a modified Valsalva experiment consisting of holding the breath in in-

spiration and making an expiratory effort with the glottis closed. This produces a great increase in the systemic venous pressure which subsides soon after the effort is stopped. During the period of increased venous pressure and distention, loosely attached thrombi are likely to break off and thus are carried to the lungs.

The *onset* of pulmonary embolization varies with the size of the embolus In cases where the emboli are small, there may be little disturbance. The patient may complain of some vague chest pain, slight cough and occasionally some hemoptysis. Pulmonary signs may be negligible or non-existent.

If the emboli are large enough to shut off larger branches of the pulmonary vessels, the condition may be associated with considerable chest pain, shock, dyspnea and a sense of suffocation. This is followed within twenty-four hours by rise in temperature to 101 degrees F. or even higher, leukocytosis, increase in the sedimentation rate of blood cells and signs of pulmonary infarction If the infarction extends to the surface of the pleura, pleural pain appearing on respiration and a pleural friction rub may occur over the involved area The onset of the attack and the subsequent course may closely simulate symptoms and signs of acute coronary occlusion with which it is frequently confused. Only careful study of the case will enable us to arrive at a proper diagnosis. The author has encountered many cases of pulmonary embolization which were erroneously diagnosed as coronary occlusion. Even the electrocardiogram may occasionally be misleading, as described elsewhere.[15]

Experimentally, De Takats and co-workers[16] have demonstrated that pulmonary embolization is associated with reflex vagal effects producing bronchiolar spasm and increased bronchial secretion which result in localized atelectasis of the lung. They believe that some of the clinical manifestations may be due to such changes They also believe that postoperative and traumatic atelectasis may have the same reflex mechanism

In all cases where pulmonary embolization does not cut off a major portion of the pulmonary arterial branches, acute cor pulmonale does not occur. Evidently a reflex protective mechanism demonstrated experimentally by Parin[17] comes into play. This consists of a reflex drop in systemic pressure due to peripheral vasodilatation and cardioinhibition caused by afferent impulses originating in the pulmonary vessels Also, the shock syndrome is a common clinical manifestation in these cases. Both of these mechanisms diminish the return blood flow towards the right heart, thus preventing overburdening of the pulmonary circulation.

In massive pulmonary embolization, with sudden occlusion of most of the major branches of the pulmonary artery, however, sudden acute pulmonary artery and right heart dilatation occurs, producing the characteristic picture of acute cor pulmonale.

The onset of acute cor pulmonale is abrupt The patient suddenly develops marked dyspnea, precordial oppression, marked cyanosis with dilatation of the veins in the neck and collapse The second sound becomes markedly accentuated and a loud systolic murmur develops in the pulmonic area. There may be a visible and palpable pulsation in the second and third left interspaces due to sudden dilatation of the pulmonary conus and artery Occasionally, a friction rub may be heard in this area. Right heart failure may ensue, producing acute liver enlargement with pain and tenderness over the liver region due to stretching of Glisson's capsule A gallop rhythm may be heard over the sternal region. Death may ensue in a few hours although some may survive even a major onslaught In the latter, slow recovery will occur if no recurring embolization takes place

If recovery occurs, there is an elevation in the temperature and in the leukocyte count within a few hours. Signs of massive pulmonary infarction develop and there may be pleural pain with a pleural friction rub on respiration. The respiratory rate is accelerated and hemoptysis usually occurs The electrocardiographic findings are fully described elsewhere.[15]

Subacute Cor Pulmonale In this rare condition the development of pulmonary artery dilatation and right ventricular hypertrophy with ultimate failure is more slow than in acute cor pulmonale. In view of the underlying pulmonary pathology of carcinomatosis the progress is much faster than in the chronic form, the usual duration being several months, and in rare cases, perhaps as long as two years

An interesting case of a girl, 20 years old with alveolar cell carcinoma is reported by Fishman and co-workers[18] The patient developed the first signs of pulmonary involvement about two years before death No evidence of pulmonary artery dilatation or cardiac changes were noted at that time During the two year period of observation, she showed progressive signs and symptoms of cor pulmonale, with marked pulmonary conus bulging, roentgenologically At necropsy, extensive atheromatosis of the pulmonary artery was noted, with intimal proliferation and narrowing of the lumina of the smaller vessels There was widespread infiltration of the pulmonary parenchyma with alveolar tumor cells The authors speculate as to the reason for the coexistence of pulmonary artery sclerosis and the pulmonary malignancy. Inasmuch as pulmonary arterial hypertension is to be expected to occur in massive arteriolo-capillary obliteration by such a tumor, it would logically explain the development of pulmonary artery sclerosis and atheromatosis The fact that pulmonary artery dilatation was not present before and that it developed during the period of two years of observation would tend to corroborate this impression.

The manifestations of subacute cor pulmonale are the same as in the acute form but, as said before, are more slow in their development. When

right heart failure ensues, cyanosis becomes marked, liver enlargement and peripheral edema are progressive. Dyspnea, of course, is an outstanding feature from the early phases due to the pulmonary involvement.

Chronic Cor Pulmonale: Here, increased intrapulmonic pressure is progressing slowly, resulting in the slow development of atherosclerosis and dilatation of the pulmonary artery, right ventricular hypertrophy and ultimate failure.

The underlying pathology is chronic pulmonary disease and chronic disease of the pulmonary arteriolo-capillary radicals mentioned before

The resulting increase in intrapulmonary arterial blood pressure throws a greater strain on the right ventricle and the major pulmonary branches. A variable degree of right ventricular hypertrophy occurs and in some cases, left ventricular hypertrophy also develops due to prolonged anoxemia of the heart muscle Spain and Handler found occasional mural thrombi in the right auricle and arterial thrombosis of the smaller branches of the pulmonary arteries. In 5 per cent of their cases, cardiac cirrhosis of the liver was present.

Clinical manifestations Two phases are recognized—the early pulmonary and the later cardiac

In the *early pulmonary phase*, the symptoms and signs are those of chronic pulmonary disease going on for many years. These may consist of chronic cough with expectoration, occasional hemoptysis, more or less dyspnea, cyanosis and physical signs of pulmonary disease. These various manifestations have periods of exacerbation and remission. During the period of exacerbation, there may be some elevation in temperature, increase in the heart rate, and other signs of acuteness of the process In addition to the pulmonary manifestations, polycythemia and clubbing of the fingers occur frequently. These develop slowly and progressively.

The appearance of many of the patients who present emphysema is characteristic They usually have a barrel-shaped chest with insufficient respiratory movements of the chest wall and more or less immobility of the diaphragm The respiratory rate is increased to compensate for the diminished depth of respiration. The breath sounds are markedly diminished in intensity, with prolonged expiration and often there are wheezing rales. Signs of localized pulmonary bronchiectasis may be present

The cardiac phase develops later in the disease when right heart failure begins to exhibit itself. It is characterized by slowly developing liver enlargement, edema of the extremities, and rise in venous pressure, described in Chapter XIII, under right heart failure The cyanosis becomes much more marked and the condition is often spoken of as "black cyanotics" The veins in the neck become distended and may show a systolic pulsation due to some degree of tricuspid insufficiency which occurs in occasional cases.

Many of the cases have a variable degree of coronary sclerosis, resulting in the anginal syndrome in addition. Precordial pain, however, may occur in these cases in the absence of coronary sclerosis, due probably to anoxemia caused by the pulmonary disease

A proper physical examination of the heart in many of these cases is often difficult to carry out due to the pulmonary pathology. The heart borders cannot be definitely mapped out and the heart sounds and any murmurs that may be present cannot be determined very clearly Careful examination, however, reveals no definite cardiac enlargement on percussion The first heart sound is greatly diminished in intensity, often being hardly audible and the pulmonic second sound is accentuated A systolic murmur may be heard over the apex in a certain proportion of cases. In an occasional case, auricular fibrillation may be present

A roentgenologic examination may give us improper information as to the exact size of the heart in cases where marked emphysema is present. This is due to the fact that the diaphragm is depressed and the mediastinum appears therefore to be oblong The cardiac silhouette assumes a somewhat narrowed and atypical shape and appears to be of normal proportional relationship to the chest, even though it may actually be enlarged The abnormal relationship of the size of the heart to that of the chest is further accentuated by the decrease in the transverse chest diameter in these cases. The only indication of right ventricular enlargement may be a prominence of the outflow portion of the right ventricle seen in the right oblique position, as described in Chapter VI.

The electrocardiogram often aids in the diagnosis of right ventricular enlargement, described elsewhere [15] In cases where chronic cor pulmonale is due to pulmonary arterial disease, the pulmonic conus is usually prominent.

The venous pressure is often elevated above normal, but in some cases and at certain periods, it may be within normal limits. There is always a variable degree of polycythemia, running at times as high as 10,000,000 red blood cells per cubic millimeter.

Differential diagnosis. Chronic cor pulmonale may resemble certain congenital forms of heart disease where no characteristic murmurs are present The differential diagnosis in most cases is easy. The absence of a history of heart disease from early childhood and the presence of chronic pulmonary disease with emphysema speak for cor pulmonale, in the presence of the signs and symptoms enumerated before. In rare cases of congenital heart disease where no history is present and where the condition is complicated by emphysema, it may be difficult or impossible to make a differential diagnosis

Prognosis. Many cases with chronic pulmonary disease may go on for

many years before right heart failure ensues, even though the right ventricle may undergo progressive hypertrophy incident to increased intrapulmonic pressure. When right ventricular failure ensues, and is uncontrollable the duration of life is short, probably several months. Some cases may live a year or two, but rarely longer. Some die suddenly. Many cases develop acute pleuropulmonary involvement which may extend to the pericardium and which results in early death.

Treatment

The treatment of pulmonary vascular hypertension and cor pulmonale is to be directed primarily to the underlying cause.

In pulmonary embolization, before an occlusion of a major branch of the pulmonary artery occurs, the source of embolization should be looked for. If due to venous thrombosis, anticoagulant therapy should be instituted at once, to prevent, if possible, further embolization. This is described in Chapter XIX. If an occlusion of a major branch of the pulmonary artery occurs *with serious circulatory and respiratory embarrassment*, bed rest, morphine, oxygen and other care is called for as in other acute vascular accidents, such as in coronary thrombosis, to be described in Chapter XX. Active anticoagulant therapy should be instituted at the same time. If a major portion of the pulmonary arterial system has been suddenly shut off death may ensue before enough time is had for effective therapy.

In subacute cor pulmonale due to pulmonary carcinomatosis we have no effective therapy. The patient is to be made as comfortable as possible by morphine and allied drugs and by oxygen when necessary.

In chronic cor pulmonale due to pulmonary disease, the underlying lung condition should receive proper attention The prevention of acute reinfection is essential. This calls for proper attention to the general health of the patient, and the avoidance of exposure to cold and infections. Change in climate may be necessary in many cases Drugs that relieve bronchial spasm and cough, such as belladonna and codeine, and, at times adrenalin may be of help In severe cases, oxygen may be useful

When the pulmonary pathology is due to syphilis, antiluetic treatment may be of value.

Later, during the phase when right heart failure has developed, treatment of the heart failure should be carried out as discussed in Chapter XIII.

REFERENCES

1 Brenner, O Pathology of the vessels of the pulmonary circulation Arch Int Med 56 211, 457, 724, 976 and 1,189, 1935

2 Spain, D M, and Handler, B J Chronic cor pulmonale Sixty cases studied at necropsy Arch Int Med 77:37, 1946

[3] Cloetta, M. In Welcher Respirations Phase ist die Lunge am Besten Durchblutet Path U Path Anat 70 407, 1912
[4] Fishberg, A Hypertension and Nephritis Philadelphia, Lea & Febiger, 1930
[5] Greenspan, E B Carcinomatous endarteritis of pulmonary vessels associated with aneurysm of pulmonary artery Arch Int Med 54 625, 1934
[6] Thompson, L E, and Gerstl, B Thromboangiitis of pulmonary vessels associated with aneurysm of pulmonary artery Arch Int Med 77 614, 1946
[7] Bedford, D E, Aidaros, S M, and Girgis, B Bilharzial heart disease in Egypt Brit Heart J 8 87, 1946
[8] Oppenheimer, B S Idiopathic dilatation of the pulmonary artery Tr A Am Physicians 48 290, 1932
[9] Gold, M A Congenital dilatation of the pulmonary arterial tree Relation to Ayerza's disease and primary pulmonary arteriosclerosis Arch Int Med 78 197, 1946
[10] Moschcowitz, E Vascular Sclerosis New York, Oxford University Press, 1942
[11] Spain, D M, and Moses, J B Thrombosis and embolism of pulmonary vessels with special reference to pulmonary vein thrombosis Am J M Sc 212 707, 1946
[12] Allen, A W, Linton, R R, and Donaldson, G A Venous thrombosis and pulmonary embolism J A M A 128 397, 1945
[13] Morton, J J, Mahoney, E B, and Mider, G B An evaluation of pulmonary embolism following intravascular venous thrombosis Ann Surg 125 590, 1947
[14] Chapman, E M, and Linton, R R Mode of production of pulmonary emboli J A M A 129 196, 1945
[15] Sigler, L H The Electrocardiogram Its Interpretation and Clinical Application New York, Grune & Stratton, 1944 P 207
[16] De Takats, G, Fenn, G K, and Jenkinson, E L. Reflex pulmonary atelectasis J A M A 120 686, 1942
[17] Parin, V V The role of pulmonary vessels in the reflex control of the blood circulation Am J M Sc 214 167, 1947
[18] Fishman, A P, Epstein, B S, and Grayzel, D M Primary alveolar cell carcinoma of the lung with pulmonary artery sclerosis and right heart failure Am Heart J 30 309, 1945

CHAPTER XIX

Disease of the Systemic Blood Vessels

THE VASCULAR system may be affected by degeneration, inflammation, and angiospasm These pathologic changes may be widespread but some vascular areas of the body are usually more involved than others. The vascular disease may result in interference with tissue nutrition and to a varying degree in tissue anoxia. Severe cases may end in tissue destruction. The clinical manifestations depend upon the extent and location of the vascular involvement.

We shall attempt to present briefly the more important forms of vascular disease and their manifestations.

ARTERIOSCLEROSIS

This is the most prevalent form of degenerative arterial disease. Everyone alive beyond middle age presents arteriosclerosis in various degrees in one or another part of the body.

Etiology and Pathogenesis

The underlying causes and modes of development of arteriosclerosis have been the subject of a great deal of discussion and experimentation for many years and the problem still remains unsolved today. The reason is that the degeneration develops slowly and stealthily over many years and although some phases can be reproduced in experimental animals in a comparatively short time, the degeneration in its entirety, as seen in the human, is not reproducible

We shall not enter the many controversial theories and the interesting experimental work that has been done to date on the etiology and pathogenesis of the disease. The reader is referred to the numerous excellent monographs and papers on the subject, particularly the volume edited by Cowdry,[1] the reviews by Hueper[2] and the monograph by Moschcowitz.[3] We shall present here a few of the more established facts.

Probably the most important factor in the pathogenesis of arteriosclerosis is heredity. There is a definite constitutional predisposition to the disease in certain individuals As Osler many years ago remarked, the "vital rubber" of the arteries with which we are born varies with different individuals and is hereditary. As clinicians, we are struck by the frequency of early development of arteriosclerosis in certain families and although it may be due largely to a particular environment in such families, it cannot be entirely explained on that basis.

Another important factor is the intravascular tension of the circulation, continuing over many years This is stressed by Moschcowitz who considers it the only cause That it is one of the main causes is evidenced by the fact that arteriosclerosis is most prevalent in cases with hypertension and that pulmonary artery sclerosis is practically never a part of systemic arteriosclerosis but occurs only in cases where there is increased intrapulmonic pressure, as in mitral stenosis, some congenital heart disease and so on. *That it is not the sole cause, however, appears to be evinced by* the fact that we often find comparatively young individuals with marked arteriosclerosis having normal or subnormal blood pressure. These cases must either be assumed to have "poor tubings" to start with, which react to normal intravascular tension in an abnormal manner, or that some additional unusual factors are operative in the production of the arteriosclerotic process in these individuals.

That overindulgence in food may be a factor is evinced by the greater frequency of the disease in obese individuals, as shown by Wilens[4] and several observers before him, although some deny it. Joslin[5] blames the occurrence of early arteriosclerosis in diabetes on excessive fat and cholesterol intake High blood cholesterin is also found in nephrosis and in some cases of nephritis and in myxedema where the incidence of arteriosclerosis is great The relationship of fat and cholesterin intake to the genesis of artertiosclerosis, however, has not been definitely established Leary[6] stresses this relationship He believes that the transportation of fat and cholesterin from the blood into the subintimal layers of the arterial wall by phagocytes is the underlying cause of arteriosclerosis and atheromatosis. However, although fat and cholesterin are present in abundance in atheromatous lesions, it has not been definitely proven that it is the primary cause of such lesions Degenerative changes caused by local circulatory disturbances in the arterial wall due to tension may be the cause of such deposits Also, increased vascularization of the arterial wall, especially in the subintimal layers, demonstrated by Winternitz and Le Compte,[7] may often result in capillary hemorrhage with the accumulation of blood in the arterial wall and may lead to local irritation, subacute inflammation and degeneration with infiltration of fat and cholesterin and later, calcium. In such cases, capillary hemorrhage in the arterial wall has also been demonstrated by Paterson[8] who found it to be the cause of intimal rupture and thrombosis

Alteration in the physico-chemical composition of the blood such as may occur in infections, intoxications, various forms of trauma and in a great many other constitutional disturbances may be a factor in the production of atheromatosis, if frequently repeated or if chronic in nature. The recent work on the microscopic study of the arteriolo-capillary circula-

tion in health and disease, summarized by Knisely and co-workers,[9] throws light on this possible mechanism. They observed that normal blood cells flow freely in these vessels without interruption, under normal conditions. In a great variety of abnormal bodily states more or less sludging of blood takes place, resulting in arteriolo-capillary plugging in various areas. This mechanism appears to be a factor, not only in the production of intravascular thrombosis, but may also interfere with the nutrition of the intima in certain parts of the large vessels by the deposition of sludges in those

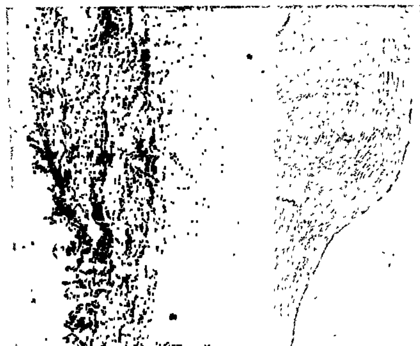


FIG 88—EARLY ARTERIOSCLEROTIC LESION OF THE AORTA Thickening of the subendothelial connective tissue of the intima

areas Further study of the physico-chemical changes of the blood may help solve many problems associated with aging

Pathology

In the early phases, thickening of the subendothelial connective tissue of the intima takes place, caused by proliferation of the wandering cells, shown in Figure 88. Later, atheromatous plaques of different sizes and shapes develop which project into the lumen of the vessel. These plaques consist of necrotic tissue and deposition of fat and cholesterin. The elastic

layer is broken and new elastic fibers develop and infiltrate the tissue Still later, the media also becomes involved These changes are shown in Figure 89. Moschcowitz found that in the decrescent or senile form, the media is apt to become thinner, while in the hypertensive type, thicker than normal Infiltration of the vessel wall with connective tissue soon takes place and there is destruction of the muscular and elastic tissue.

In the final stages, the entire thickness of the vessel wall is involved by degeneration, shown in Figure 90 The atheromatous plaques rupture into the lumen of the vessel and result in crater-like ulcers In some areas,



FIG 89—ATHEROMATOUS PLAQUE OF AORTA Necrotic changes, fat deposit and cellular infiltration of intima There are also some degenerative changes of the media × 68

there is marked infiltration of the atheromatous plaques with calcium, resulting in hardening and roughening of the intimal layer, thus forming a focal point for a thrombus formation.

The gross appearance of the vessel in the late stages is that of increased width and marked tortuosity resulting from stretching in the longitudinal and circular directions The lumen, however, is irregular with areas of marked narrowing and in some places it is eccentrically placed due to protrusion of the thickened intima. Complete obliteration of the lumen may occur slowly by the progressive growth of a plaque and thrombus deposit with organization, or it may develop suddenly as a result of large

thrombus formation or a broken off plaque which is carried as an embolus and occludes a smaller caliber artery lower down. An interesting example of the former is represented in Figures 91 and 92.

There is a form of arteriosclerosis, described by Monckeberg,[10] which consists predominantly of primary necrosis and calcium deposit in the media of the artery, the intima being only slightly affected. Often, the media undergoes osseous changes resulting in the narrowing of the vascular lumen. The condition frequently occurs in association with the usual type of arteriosclerosis



FIG 90—MARKED DEGENERATION AND PATCHY CALCIFIC INFILTRATION AFFECTING THE ENTIRE THICKNESS OF THE AORTIC WALL. The surface of the intima is broken by a projected atheromatous and calcific plaque × 32

Clinical Manifestations

The effect of arteriosclerosis, as said before, is dependent upon the degree of its interference with the nutrition and oxygenation of a given structure or organ, as well as upon the rapidity of onset of such interference. Arteriosclerotic changes affecting the large vessels, with little involvement of the arterioles, may be entirely asymptomatic for many years Widespread sclerosis of the smaller arteries or of the arterioles in a given structure or organ, on the other hand, will result in a varying degree of ischemia and nutritional disturbances depending upon the extent of the development of a

collateral circulation This is also true if a large vessel has undergone obstruction by a growing atheromatous plaque The flow of blood through that vessel will be slowed and the blood supply will be diminished in the affected area. Angiospasm is an important factor in the production of symptoms, especially in cases of advanced arteriosclerosis This may occur intermittently under various provocative causes.

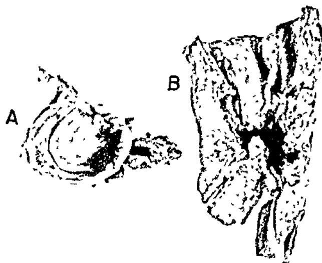


FIG 91 —OLD, OBLITERATIVE THROMBOSIS OF THE AORTA AND THE COMMON ILIAC ARTERIES A, cross section of the aorta, B, lower part of the aorta and parts of the common iliac arteries Both A and B are reproduced in their natural sizes Note the laminated appearance of the organized thrombus in A

From a male, 54 years old with marked hypertension and generalized arteriosclerosis He sustained a hemiplegia two years before death, and for six years he was subject to pain in the lower extremities with absent pulsation of the palpable vessels, marked progressive coldness and blueness of legs He died two hours after an acute episode of epigastric pain due to a fresh thrombus in the abdominal aorta extending to the openings of the renal arteries

The following is a short resume of involvement of the more important structures and organs

The Heart: Coronary sclerosis may produce progressive myocardial ischemia resulting, eventually, in myocardial fibrosis and fibrotic changes of the various valves The manifestations of such involvement are mainly those of the anginal syndrome but in some cases, myocardial failure may eventually occur, as described in Chapters XIII and XIV The various

various murmurs as described in Chapters IX and XXIV. Acute oc
sions frequently take place which may result in myocardial infarction
the symptom-complex, described in Chapter XX.

The Brain: Arteriosclerosis in this organ may result in ischemia
encephalomalacia which produce a long train of characteristic signs
symptoms There is a tendency to forget recent events while old expe
ences are remembered Dizziness, vertigo, transitory palsies, aphasias a
occasional syncopal attacks may occur. Intellectual deterioration, em

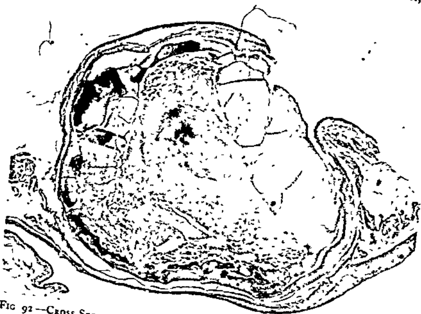


Fig 92—Cross Section of a Thrombosed Common Iliac Artery from Fig. 91 The various layers of the thrombosis are of different ages The portion close to the vessel wall shows organization and areas of calcification The central portion consists of layers of thrombosis of more recent origin Recanalization is noted in some sections

tional instability and dementia often develop. Hemiplegia is frequent, especially in the presence of hypertension when the condition is often due to hemorrhage We occasionally also observe cases with epileptic seizures where no other cause than cerebral arteriosclerosis could be found

Renal Arteriosclerosis: This may produce diffuse nephrosclerosis Many of these cases may be asymptomatic in the early phases. In an occasional case, there may merely be a trace of albumin and a few casts in the urine. Later, however, signs of renal insufficiency may develop.

Arteriosclerosis of the Pancreas. This may result in interference with the

secretion of insulin and the pancreatic enzymes. The former may account for the frequent occurrence of diabetes and the latter for digestive disturbances in the older age groups

Retinal Arteriosclerosis The severe form of retinal arteriosclerosis usually occurs in association with hypertension and may result in neuroretinitis. Transient amaurosis may occur due to retinal angiospasm Retinal artery thrombosis may produce permanent blindness

Arteriosclerosis of the Mesenteric Vessels This condition may be associated with angiospasm and symptoms of so-called abdominal angina Digestive disturbances might also develop. Mesenteric thrombosis may occur, resulting in intestinal gangrene

Peripheral Arteriosclerosis. The obliterative form of arteriosclerosis affecting the extremities, results in a train of symptoms and signs by which it may be easily diagnosed. In the early phases, the patient may complain of coldness, numbness, or heaviness in the involved extremity with a sense of fatigue or weakness and a dull or cramplike pain in the muscles at night In some cases, this spontaneous pain may be very excruciating, even in the absence of marked tissue changes The characteristic pain, however, is that which occurs with varying severity on muscular activity. If the main arteriosclerotic changes are in the lower extremities, walking brings about pain in the arches, calf muscles and occasionally in the thighs The distance the patient can walk before the onset of such pain is a good measure of the degree of insufficiency of the arterial blood supply The condition is spoken of as "intermittent claudication" and is analogous to effort angina in coronary insufficiency, described in Chapter XIV

The physical findings vary with the degree of local interference with the circulation. In the early phases, there is more or less atrophy of the skin, and the nails may show some brittleness and stunted growth On elevation of the limb, the skin of the toes and foot becomes pale and on lowering it, a reddish-cyanotic hue appears Later, some degree of muscular atrophy may be detected which is often easily determined by comparing the measurements of the circumferences of the affected and the non-affected or less affected limb Small ulcers may develop about the toes, heel or other parts of the foot, ankle or over the tibial surface. They are usually dry and of grayish color, the base often being black. If they become infected, a red zone develops around the ulcerated area and the ulceration becomes moist Ulceration usually follows a varying degree of trauma, such as careless cutting of a corn, or nails, some blows and so on Larger areas of gangrene usually follow the closure of a major vessel

The palpable arteries may be tortuous and not easily compressible Patchy calcification may be detected in some cases in a varying degree The pulsation of the dorsalis pedis and posterior tibial arteries may be greatly diminished or entirely absent. If present, however, it does not rule

out circulatory insufficiency as the occlusion may be in some of the smaller arterial branches. We often observe a waxing and waning of the pulsation in a given artery at various intervals due to intermittent angiospasm.

The temperature of the affected portions of the limb is lower than that of the normal limb. This can be easily detected by the examiner's hands. For more accurate study, the thermocouple may be employed. In the determination of the skin temperature, it is important to examine the patient in a comfortably warm room. Cold air produces vasoconstriction and a subnormal skin temperature, even in normal individuals. The average normal skin temperature varies between 85 and 93 degrees Fahrenheit, in a comfortably warm room. In obliterative arteriosclerosis, the temperature in the affected limb may be as low as 70 degrees Fahrenheit or even less, in the same room.

The vasospastic element may in some cases be so severe as to be more of a cause of destructive tissue changes than the structural occlusion itself. To determine how much vasospasm is responsible for the various manifestations, certain tests have been devised One is the *reflex vasodilatation test* This consists of applying considerable heat to a given part of the body Ordinarily, this produces warmth of other parts such as the limbs, due to reflex vasodilatation If the skin temperature in the limb affected by obliterative arteriosclerosis does not become warmer, the occlusion is presumed to be structural Another test is the induction of fever by intravenous typhoid injection If there is no rise in the skin temperature of the affected limb, the vasospastic element is excluded. A third test is the occurrence of subjective improvement due to vasodilatation by paravertebral alcohol block. Freeman and co-workers[11] mention delayed blanching of the extremity on elevation; a cold and clammy foot or hand, a cyanotic mottling of the digits; and, a constriction of the superficial veins, additional evidence of the presence of a vasospastic element

Oscillometric readings are of help in determining the patency of major vessels. The point of maximum oscillations of the dial at whatever blood pressure level it occurs should be used. Normally, the *minimum oscillation* at the ankle and wrist is one degree and higher up, two degrees. Figures lower than these indicate circulatory interference The maximum oscillation may, of course, normally be much higher Readings should always be obtained in a comfortably warm room to eliminate the vasospastic element.

Roentgenologic examination of the affected limb may help determine the presence of more or less calcification of the involved arteries It does not help determine the patency of the vessel unless *arteriography* is performed. This consists of x-ray examination after injecting a radiopaque material into the suspected artery.

The histamine flare test is occasionally used to determine the local circula-

tory state, especially that of the skin. About 1½ minims of 1–1,000 histamine solution is injected intradermally at various levels of the affected limb A flare normally develops about 1 to 2 centimeters wide. If small or absent, it indicates local circulatory impairment

Acute Arterial Occlusion

This may result from embolization or from sudden development of thrombosis at the site of an inflammatory or atheromatous portion of an artery. Embolization may occur even in a normal vessel when its source may be a dislodged atheromatous plaque, and more often, dislodged thrombi forming in the left heart in auricular fibrillation or at the site of myocardial infarction. In rare cases of parodoxical embolization, the source may be thrombosis in any of the systemic veins Nygaard and Brown[12] reported 5 cases of sudden arterial occlusion due to thrombophilia or increased coagulability of the blood

The symptoms and signs of acute arterial occlusion depend upon the area of the body involved and the size of the vessel occluded Most acute major arterial occlusions in any part of the body are associated with severe pain and shock, as described under coronary occlusion in Chapter XX The pain, of course, is usually referred to the region of the body involved A major occlusion is followed later by rise in temperature, leukocytosis and increased sedimentation rate The subsequent course is dependent upon the amount of acute tissue destruction and the area destroyed

In some cases of arterial occlusion, pain may be minimal or entirely absent The outstanding early symptoms may be extreme dizziness, faintness, collapse, nausea, a sense of oppression and a variety of other manifestations depending upon the location of involvement Many cases are misdiagnosed or overlooked because, as Conner[13] said, the condition is not borne in mind and in many cases of occlusion involving various internal organs, no clean cut clinical pictures have as yet been worked out This is further complicated by the fact that the onset may be gradual rather than acute, especially where the occlusion is due to thrombosis

Acute occlusion of a coronary or cerebral vessel is, in the majority of cases, easily diagnosed Acute occlusion of a mesenteric vessel, involving a large branch should also offer no difficulty in diagnosis. It is characterized early by severe abdominal pain and cramps with more or less shock but no localized rigidity or severe tenderness which are present in acute abdominal visceral disease. Within six to twenty-four hours, however, signs of peritonitis develop, when gangrene of the intestines or of the omentum develops. The author has observed four cases in which a correct clinical diagnosis was made and proved either at autopsy or at operation. In one, mesenteric thrombosis and intestinal gangrene occurred after recovery from left heart failure in arteriosclerotic, hypertensive heart disease. In an-

other, mesenteric embolization and intestinal gangrene occurred twelve days after a coronary occlusion. In a third, mesenteric artery thrombosis followed two weeks after splenectomy and in a fourth there was mesenteric embolization in a case of auricular fibrillation and mitral stenosis. There are instances where occlusion occurs in small branches of the mesenteric vessels, not followed by gangrene and the secondary manifestations of peritonitis. Tympanitis may be an outstanding feature in such cases

It is beyond the scope of this volume to go into the various manifestations of acute arterial occlusion affecting various organs or structures of the body. We shall merely describe briefly the manifestations of *arterial occlusion of the lower extremities* which is quite prevalent The onset here, is usually characterized by agonizing pain In some cases, however, there may be little or no pain. There may be merely sudden onset of numbness and tingling sensation, local paresthesia or anesthesia and loss of muscular power. Marked coldness is present in all cases. The characteristic pallor, mixed with a cyanotic hue develops and massive gangrene may follow.

In many cases, there is an element of severe angiospasm of the occluded as well as of the adjacent vessels which contributes greatly to the symptomatology The amount of pain and color changes as well as the extent of subsequent gangrene are good measures of the degree of angiospasm and the amount of collateral circulation.

Treatment

The treatment of arteriosclerosis is primarily preventative. Once the condition has developed in a certain area of the body we have no means of curing it All we may hope to accomplish is to slow its progress so as to allow time for the development of a good collateral circulation to compensate for the insufficient blood supply resulting from the sclerosis

The preventative measures employed are the same as those outlined under hypertension in Chapter XVII.

The treatment of the effects of arteriosclerosis varies to some extent with the structure or organ predominantly involved, and with the rapidity of onset of such involvement. Slowly progressing arteriolar obliteration in any organ or structure may result in some concomitant increase in the collateral circulation, so that the function of the involved organ or structure may not be seriously affected for a variable length of time. An acute occlusion affecting a fairly large blood vessel in an area where the collateral circulation has had no time to develop may result in acute tissue destruction and serious consequences.

We shall leave the therapy of the various organs that may be affected, especially the heart, to other sections of this text, and confine ourselves to the therapy of obliterative arteriosclerosis of the lower extremities.

In the early stages, it is essential that the extremities have relative rest.

The amount of walking should be limited. As soon as any tiredness, aches or pains of the muscles develop, walking must be stopped. The feet and toes must be kept clean, and care should be taken in clipping the nails or in removing corns. The shoes must not be tight, and local pressure on any portion of the feet or toes must be strictly avoided. The legs and feet should be kept warm

The use of tobacco is to be strictly prohibited. Liquor, however, is beneficial in these cases and should be used in moderation, especially when pain is protracted

In an attempt to improve the collateral circulation, exercises devised by Buerger[14] may be employed. The patient lies flat on his back and elevates his feet for two minutes, then lowers them for one minute and rests for two minutes. These movements may be performed four or five times in the morning, afternoon and evening.

Another means that may be employed, in an attempt to improve the circulation, is the use of warm sitz baths The temperature of the bath should never exceed 100 degrees Fahrenheit, and in many cases a lower temperature is preferable It may be beneficial to add epsom salt to the water.

The use of deproteinated pancreatic extract by intramuscular injection may occasionally be of value One such proprietory preparation, Depropanex, may be given in doses of 2 cc., two or three times weekly for several weeks. If no relief is obtained it should not be continued

An acute vascular occlusion, either embolic or thrombotic, calls for complete bed rest. The affected limb should not be elevated to avoid further diminution of blood flow. Papaverine hydrochloride, two or three grains intravenously may give relief from pain by reducing the associated angiospasm. In some cases where the pain is very severe and is not relieved by this drug, morphine, pantopan or dilaudid may be required The limb is to be kept warm by wrapping it in cotton An electric cradle may be used for additional warmth and to avoid the pressure of bed coverings, but no more heat than about 95 degrees Fahrenheit should be employed.

If gangrene develops, its extent and the circulatory condition of the adjacent tissues are factors to be considered to determine whether surgery is indicated. If the gangrene is rapidly spreading, amputation high above the gangrenous area will be necessary in most cases. If strictly limited and well demarcated, conservative therapy is to be used. If the gangrenous portion is dry and hard, local application of moist non-irritating dressings, such as weak boric acid solution should be used. If severe secondary infection develops, penicillin should be employed.

Sympathectomy may be of great value in those cases where there is a marked vasospastic element superimposed upon the structural interference

with the vascular supply. It relieves pain and it improves the circulation by producing vasodilatation. Freeman and co-workers[11] stress the fact that if little or no evidence of vasomotor activity is present sympathectomy is not only useless, but may prove harmful by inducing the onset of gangrene They suggest the use of Atlas' signs to determine the contraindication to sympathectomy. These are severe extensive arterial occlusion, rapid blanching of the extremity on its elevation and atrophy of the skin and superficial tissues

Thromboangiitis Obliterans

This thrombo-inflammatory vascular disease was first described by Buerger[15] and is, therefore, named after him. In most cases, it affects the lower extremities, but the upper extremities are not spared In fact, the disease is known to involve, occasionally, any vessel of the body Taub[16] cites 26 cases from the literature where the coronaries, aorta, the cerebral, celiac axis, mesenteric, spermatic, carotids and iliac vessels were affected Davis and Ferret[17] report 11 cases of cerebral involvement, 9 of which had no involvement of the extremities

Etiology The underlying cause is unknown Tobacco appears to be one of the predisposing or aggravating factors It occurs most frequently in young males between 20 and 40 years of age, but it may occur, also, in older persons There is a definite racial predisposition, being most common among Jews, although other races are not exempt, as described before [18] Extreme cold, strain and trauma precipitate an attack of active symptoms in some cases.

Pathology· The essential changes consist of patchy, migrating thrombosis of the arteries and veins with inflammatory reaction of the vascular walls Intimal proliferation with giant and round cell infiltration is seen microscopically Each area involved is about 5 to 10 centimeters long, and the portions between the involved areas may be normal Organization takes place by richly vascularized connective tissue which may involve the entire thickness of the vessel, its sheath and nerves In some places, recanalization occurs The changes are illustrated in Figures 93 and 94

Clinical Manifestations· The symptoms here are the same as in obliterative arteriosclerosis, described above The manifestations in thromboangiitis obliterans, however, may often subside for periods of months or years, thus differing from obliterative arteriosclerosis. Other distinguishing points are its appearance earlier in life and the occasional presence, in this condition, of superficial thrombophlebitis. In cases where the disease first manifests itself in the arteriosclerotic age, the clinical differential diagnosis from obliterative arteriosclerosis is very difficult.

Prognosis· In most cases, it is almost impossible to foretell what the

outcome will be. Spontaneous amputation of the gangrenous part, with recovery of good function of the remainder of the limb, may occur in individuals who appear to be hopeless. On the other hand, some cases that appear to be mild, may suddenly develop severe symptoms with progressive and extensive spread of gangrene, requiring early amputation Remissions extending over months or years are frequently observed, with practically no symptoms.

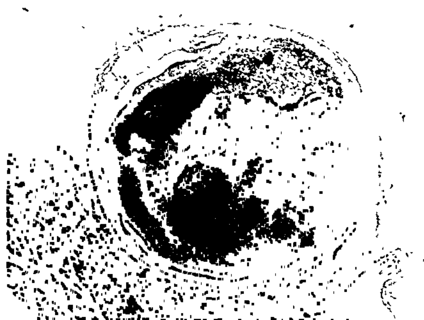


Fig 93—Thromboangiitis Obliterans Cross section of popliteal artery in involved area From a male 45 years old

Treatment: The treatment of thromboangiitis obliterans is practically the same as in obliterative arteriosclerosis Massive intravenous injections of sodium citrate or saline solution and copious ingestion of fluids have been used in the past with apparently good results. However, inasmuch as the disease has a tendency for spontaneous remissions, and there is a marked psychogenic element of suggestion, the value of any of these methods is questionable. Intravenous typhoid injections apparently do give some relief in an occasional case by inducing vasodilatation. Lumbar sympathetic ganglionectomy may also be used for the same reason in those cases where there is marked associated angiospasm, as discussed under obliterative arteriosclerosis.

Periarteritis Nodosa

This is a comparatively rare inflammatory arterial disease which, according to Schreiber,[19] was apparently first recognized in 1755 by Michaels and Matani It has received, however, the greatest attention within the last three decades. According to Harris and co-workers,[20] only 101 cases were reported in the English literature, and a total of 300 cases in the entire world literature up to 1938.



Fig 94—Thromboangiitis Obliterans, High Power Marked intimal proliferation, round cell and giant cell infiltration of the thrombosed area, with organization and richly vascularized connective tissue, involving the entire thickness of the vessel wall Two large areas of recanalization are seen × 75

Etiology· The underlying cause is not known Streptococci and filterable viruses have been blamed, but not proven In a recent review of the literature, Diaz-Rivera and Miller,[21] found that allergy is considered the most acceptable cause by most writers on the subject Various superadded infections, may perhaps, be contributory causes.

Pathology· The disease affects mainly the walls of the medium sized and small arteries in widely scattered areas of the body. Grossly, the affected artery often shows small projecting nodules, which vary in size up to 3 millimeters, and are either coalescent, or may be separated at intervals of 1 to 5 millimeters Microscopically, the adventitia and media are infil-

trated with polymorphonuclear leukocytes, eosinophiles, and mononuclear cells Medial necrosis is often prominent. There is also marked perivascular infiltration. Arterial thrombosis with hemorrhage and anemic infarction occur in various areas Organization or recanalization of the thrombosed vessels may occur. The various vascular inflammatory changes are in different stages of development and distribution with intervening normal vessel wall These are fully described in the report

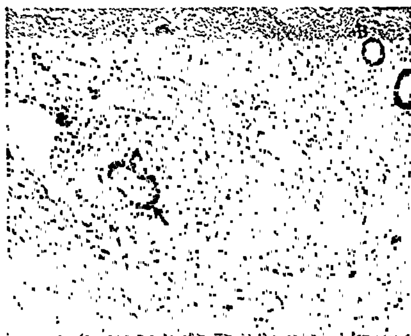


FIG 95 —PERIARTERITIS NODOSA FROM A SECTION OF THE APPENDIX Acute inflammatory infiltration and medial necrosis in the wall of a small artery, A Infiltrative process extends into the mucosa, B × 160

of five cases by Banowitch, Polayes and Charet.[22] Figure 95 is from their paper.

Clinical Manifestations These are very protean in nature because of the widespread involvement of various parts of the body The disease usually runs a subacute, moderately febrile course The symptoms and physical findings depend upon the parts of the body which are most involved at any given time The disease may resemble trichinosis, peritonitis, cholecystitis, acute gastro-intestinal affections, coronary insufficiency, rheumatic fever, miliary tuberculosis, acute cerebrospinal, pulmonary, renal or inflammatory cardiac disease. The onset is usually gradual with severe weakness

and loss of weight. Tachycardia is a constant manifestation. Other symptoms are those that may occur in any of the above conditions

Diagnosis: The diagnosis is often difficult to establish It should be considered in any case that shows diverse manifestations of subacute infectious disease lasting several weeks to months.

In a small proportion of cases, subcutaneous nodes appear in various parts of the body, especially in the extremities. These, if present, are diagnostic and are valuable for biopsy study. Eosinophilia is another diagnostic feature Its occurrence, however, is not constant

Prognosis. The disease is practically always fatal, usually within four months after the onset. In milder cases, it may last as long as two years. In the series of 101 cases reviewed by Harris, 5 were known to have recovered.

Treatment There is no specific treatment for this disease. Bed rest, proper nutrition, the vitamins and symptomatic therapy are all we can offer with our present day knowledge of the disease.

Functional Vascular Disease

It has been shown before that structural vascular disease is frequently associated with angiospasm due to local irritation and to reflex effects. In some cases we may also observe local arteriolo-capillary dilatation as a reaction to local injury.

There are rare forms of functional vascular disturbances affecting local areas, which are usually unassociated with demonstrable structural disease of the vessels. Three recognized forms are Raynaud's disease, acrocyanosis and erythromelalgia.

Raynaud's Disease

Definition: This disease usually effects the hands, feet and rarely other parts of the body. It is characterized by intermittent attacks of marked pallor followed in some cases by cyanosis, trophic changes of the skin and nails, and in extreme cases by gangrene.

Etiology The underlying causes are unknown Some of the known provocative factors are exposure to cold, local strain and trauma of the affected parts, and emotional disturbances There is evidently an exaggerated vascular response to stimulation in these cases which is ineffective in normal individuals

Pathology In the early stages, the affected arterioles undergo severe spastic constriction but show no structural changes. As a result of the arterial spasm, no blood enters the capillaries and the affected part assumes a waxy pallor. Inasmuch as the larger arteries, such as the radials, do not share in the spastic process, the pulse in such arteries is not affected. In

some cases, a slight leakage of blood occurs from the venules into the capillaries resulting in mottling cyanosis which is added to the pallor With the cessation of the arteriolar spasm, the capillaries are suddenly filled and become markedly dilated, resulting in unusual redness of the affected part

In cases where the spasm is unduly prolonged and cannot be overcome, atrophy and even gangrene of the tissues ensue due to local interference with nutrition and anoxemia

Naide and Sayen[23] have demonstrated that spasm of the veins as well as of the arteries occurs in the majority of cases of Raynaud's syndrome In some cases, venospasm predominates The clinical manifestations depend upon the predominance of one over the other. Scleroderma often accompanies this condition and may be widespread.

Clinical Manifestations These vary with the severity of the disease Some cases never progress beyond the spastic stage. Such cases merely show intermittent attacks of marked waxy pallor of the fingers of both hands, the toes of both feet, the ears or of all these parts. If venospasm is marked, some degree of cyanosis will be mixed with the pallor The affected parts feel numb, cold and somewhat painful Recovery from spasm is characterized by flushing of the affected part resulting in increased warmth

If trophic changes occur which usually affect the tips of the fingers, the involved areas may become very painful Marked gangrene is a rare occurrence

To rule out other conditions that may simulate Raynaud's disease, Allen and Brown[24] summarize the following criteria in the diagnosis of this disease. Gangrene and trophic changes are limited mainly to the skin, the involvement is symmetrical and bilateral, there are no occlusive lesions of the larger arteries; and, intermittent color changes usually precede the trophic disturbances by months or years

Carp[25] reports a case of Raynaud's disease with apparent cerebral involvement and quotes several other cases from the literature. They are characterized by recurring hemiplegia with paralysis, presumably due to cerebral angiospasm.

Treatment The patient must be warned against exposure to cold, as well as to local trauma and other irritations to the extremities. The use of tobacco must be strictly prohibited Emotional disturbances of any kind must be avoided In serious cases, change to a warm climate may be necessary. Reassurance is important. Contrast baths may prove to be of value. The hands are dipped alternately in hot and cold water, for various periods.

Duryee and Wright[26] report favorable results in this and other circulatory

disturbances from the use of mecholyl iontophoresis, originally described by Kovacs.[27] The reader is referred to the original reports by these authors for the description of this method.

In serious cases, perhaps the best relief may be obtained from ganglionectomy.

Acrocyanosis

This local vascular disturbance is characterized by dilatation of the arterioles of the hands and feet resulting in cyanosis which is mottled in some places. The dorsal surfaces of the affected parts are dry and the volar are very moist. Pressure applied to the affected part produces a white spot which disappears slowly. In severe cases, some edema of the involved areas may be present.

In most cases, the condition develops on cooling the body surface In warm environment, the skin returns to normal In severe cases, the condition may persist even in warm air.

The disturbance appears to be due to an exaggerated response of the arterioles to cold stimulation. Normally, when the skin is greatly cooled, it becomes more or less blue, due to arteriolar constriction which produces local stasis and excessive oxygenation of the capillary blood. In this disease, the process is more marked and may appear under circumstances which do not affect a normal individual

The underlying cause or causes of the disease are not known. Various factors have been blamed but not proved, such as endocrine disturbances, avitaminosis, psychogenic factors, autonomic nervous system imbalance and others Cold appears to be a definite provocative factor. It is not definitely established where the disturbance is, whether in the vessel wall itself or in its vasomotor control Lewis[28] believes the disturbance is in the former and White,[29] in the latter

There is no specific therapy for this condition. All factors that produce angiospasm must be avoided The general health of the patient must be improved if it is below par All emotional upset must be avoided.

Erythromelalgia

This condition is characterized by an uncomfortable feeling and an increase in the skin temperature affecting any of the extremities in otherwise healthy individuals The sensation is described by the patient as sticking, aching, prickling and burning, most often localized in the tips of the toes, ball of the foot and in corresponding parts of the hand It may, however, occur in other parts of the legs or arms The symptoms may be reproduced in these individuals by raising the skin temperature The amount of warmth necessary to produce the abnormal sensation varies in different

individuals and in the same individual in different parts of the extremity The condition is due to an abnormal increase in vasodilatation and a hypersensitivity of the skin.

No particular method of therapy is of any specific value here The patient must avoid too much warmth Any of the analgesics, especially the salicylates may be tried, when the symptoms are distressing.

THROMBOPHLEBITIS

Thrombophlebitis is a very serious affection of the veins because the thrombi frequently serve as sources for embolization.

Etiology

The underlying causes are numerous, and some of them are not as yet understood. Phlebosclerosis and varicocities may be predisposing factors, in some cases In others, direct injury to veins during surgical procedures, obstetrical deliveries and severe accidental bodily trauma are underlying causes In still others, prolonged enforced muscular relaxation may result in venous stasis and thrombosis, followed by inflammation. This is observed in postoperative cases and in subacute and chronic debilitating disease where prolonged bed rest is enforced Infection of the veins undoubtedly plays a role in many cases Some infections may produce a suppurative type of thrombophlebitis with septicemia and pyemia following Finally, alterations of the state of the blood, such as sludging, described before may be a factor This may occur especially after a surgical operation where some degree of shock may be present, associated with hemoconcentration, increase in the number of platelets and an increase in the amount of fibrinogen in the blood

Pathology

In some cases, the inflammatory changes of veins are believed to occur first and thrombosis is the result of the inflammation In others, thrombosis is believed to occur first as a result of stasis or physico-chemical changes of the blood and secondary inflammatory changes follow. The latter condition is often spoken of as phlebothrombosis with secondary inflammation

The pathologic changes that take place in the process of thrombophlebitis from its inception to the advanced and organized stage are not fully known Nearly all cases show more or less inflammation of the intima, media and adventitia of the involved vein.

The thrombosis usually consists of alternate irregular layers of red cells and fibrin mixed with thrombocytes and leukocytes. This would indicate that the development of the clot is in the form of slow deposits of layer

upon layer. Organization usually begins early, perhaps within forty-eight hours after the onset of thrombophlebitis and fibroblastic replacement occurs within a few weeks. During this period, some of the thrombosed masses which have not organized, have liquified and have been removed by the blood stream. Recanalization of the lumen with or without fibrosis of the vessel wall thus takes place in many cases In others, complete organization of the thrombosed mass, including the wall occurs, resulting in a thick cord.

Thrombophlebitis is associated in many cases with a varying degree of spasm of the local arteries and veins According to DeSansa,[30] the veins contain afferent sensory pathways and vasomotor components Mechanical or chemical irritation of any vein results in pain. In thrombophlebitis, vasospasm extends far beyond the area of venous involvement. Ochsner and DeBakey[31] observed that vasospasm in thrombophlebitis increases the filtration pressure and produces a relative anoxia of the capillary endothelium with a diminution in the flow of lymph These factors result in a varying accumulation of perivascular fluids and edema often seen in areas of thrombophlebitis The edema may also be due partly to the venous obstruction itself

Clinical Manifestations

These depend upon the location of thrombophlebitis In the great majority of cases, the involvement is in the lower extremities According to Hunter and co-workers,[32] as well as other authors, the process begins here in the deep vessels of the calf and ascends progressively upward *Pain* and *tenderness* in this region may be an *early symptom*

Early signs, often present, are tenderness in the calf muscles, low grade unexplainable elevation of temperature, increase in the pulse rate and, perhaps, symptoms suggestive of some pulmonary embolization These should make one suspect the existence of deep seated thrombophlebitis of the lower extremities

To elicit calf tenderness, the calf is firmly compressed from side to side The degree of tenderness produced corresponds to the amount of involvement Of course, such conditions as myositis or neuritis must be ruled out The so-called Homan's sign, consisting of pain elicited by forcible dorsoflexion of the foot is another diagnostic test.

Neuhof[34] stresses the presence of infiltration in the deep calf muscles which may be used as a sign It is elicited by having the patient rest his heels on the bed, flex the knees and relax the calf muscles. Thickening felt deep in the gastrocnemius, with tenderness in that area is considered a positive sign

As the process progresses, more or less edema begins to appear in the

lower extremity. In the early phases, before superficial edema is visible and palpable, deep seated edema may occur. This may be determined by comparing the measurements of the circumferences of the involved and uninvolved legs. The former will be found to be greater If the process extends to the superficial veins, the diagnosis is easily made Tenderness, redness and cord-like feel of the involved veins can be readily detected Superficial edema in such cases is frequently present

Deep seated thrombophlebitis in the pelvic veins cannot be diagnosed with certainty. The condition may be suspected in the presence of deep seated pelvic pain in postoperative and postpartum conditions with some elevation in the temperature, increased heart rate and evidence of recurring pulmonary embolization.

Thrombosis of the inferior vena cava, if long standing, will result in marked dilatation and tortuosity of the superficial thoracic and abdominal veins

Thrombosis of the hepatic veins is comparatively rare and presents certain manifestations which may, at times, be used in its recognition, if the condition is borne in mind In a review of twenty cases by Kelsey and Comfort,[35] sixteen presented it as an incidental finding without characteristic clinical manifestations In four cases, however, the thrombosis itself was responsible for the symptoms. In the acute phase, pain, shock, cyanosis and acidosis are present In chronic occlusion, the mechanical effects of obstruction are hepatosplenomegaly, ascites and visible distention of the superficial veins indicative of the presence of a collateral circulation The chronic stage may show exacerbation and remission of acute symptoms

Venography may be of help in questionable cases This consists of injecting diatrast in any of the superficial veins below the ankle and making stereoscopic x-ray exposures at frequent intervals Baker[36] analyzed 1027 venograms performed in normal individuals and in various pathologic cases He pointed out that satisfactory information may be obtained in 60 to 90 per cent of cases

Treatment

Thrombophlebitis requires prompt and efficient therapy to prevent possible serious pulmonary embolization. If the condition is mild and develops spontaneously without any definite cause, conservative therapy may be tried for a short time, watching carefully its effect. If it occurs postoperatively or during prolonged bed rest in any illness, or when signs of embolization appear, more active therapy is called for

Conservative Therapy: The best form of conservative therapy is, perhaps, that suggested by Meyer[37] A medicated contura bandage is applied

loosely over the affected limb and a three inch wide pressoplast bandage is applied over it with strong nonconstricting pressure. The foot, leg and thigh are covered, but not the knee Walking is advised as much as possible, but not standing Immediate relief of pain and the reduction of edema may be observed. The author has found that pulmonary embolization is nearly always prevented by this means.

Active Therapy This consists of the use of anticoagulants and venous ligation With greater experience in the use of anticoagulants in the past few years, ligation as a therapeutic measure is being done less frequently The controversy as to which is the superior method of therapy, however, is still going on between the surgeon and the internist

The author believes that careful anticoagulant therapy should certainly be used first, and if recurring embolization persists, ligation is to be resorted to in addition The advantages of anticoagulant therapy are that it spares the patient additional trauma due to operation and that it may prevent the extension of thrombosis to the pelvic veins or the development of thrombosis in the other leg Such conditions can not be effected by venous ligation Ligation of the inferior vena cava may prevent embolization from pelvic vein thrombosis, but it is a major operation, and can not be performed in some seriously sick individuals

The disadvantage of anticoagulant therapy is that it may, in some cases produce serious and even fatal hemorrhage. This is apt to occur particularly where the coagulation and prothrombin time are not done repeatedly and carefully by a trained laboratory technician Even under most careful supervision, hemorrhage may, at times, occur In a series of 1686 postoperative cases treated by dicumarol, Allen[38] found an incidence of minor hemorrhage in 3 1 per cent and of major hemorrhage in 1 9 per cent Two deaths occurred from hemorrhage On the other hand, the author estimated that 73 lives were saved and 211 patients were spared the experience of venous thrombosis and pulmonary embolization in this series of cases, by the dicumarol He concludes that although heparin and dicumarol have deficiencies which call for continued search for an ideal anticoagulant, they are fairly satisfactory for clinical use

Choice of the Anticoagulant The present anticoagulants in use are heparin and dicumarol

Heparin has the advantage over dicumarol of being quick acting and in its quick cessation of action When given intravenously its effects appear within a few minutes and disappear about three hours after the injection Hence where anticoagulant therapy is urgent, this is the drug of choice. Also, because of the rapid subsidence of its action, there is no danger of severe, prolonged bleeding It has a disadvantage in that it can not be used orally, but has to be given parenterally If administered intraven-

ously by the continuous drip method it is costly, time consuming and of extreme inconvenience to the patient, and may produce inflammation and trauma of the vessel wall

The introduction of the subcutaneous method of injection by Loewe and co-workers[39] has somewhat facilitated its use The preparation they use consists of the sodium salt of heparin incorporated in the Pitkin menstruum The disadvantage of their method, however, is that it produces considerable local pain, swelling and tenderness and is associated with fever

Stats and Neuhof[40] recently described a new preparation of heparin which can be given intramuscularly *It consists of a concentrated aqueous solution*, each 1 cc containing 100 milligrams of heparin. The dosage used varies somewhat in different individuals and is determined roughly by the body weight A person weighing 100 to 130 pounds may receive 100 milligrams every eight hours Heavier individuals require larger doses The maximum daily dose should not exceed 450 milligrams Patients weighing over 170 pounds may get one milligram per pound of body weight as a first dose and 0 5 to 0 7 milligrams per pound at eight hour intervals thereafter The coagulation time should be maintained at eighteen to twenty-four minutes If it is found at any time to be over twenty-four minutes, a smaller dose is given, or the injection is postponed for two hours. The greatest prolongation of the coagulation time is observed four to six hours after an injection when it varies between twenty-five and sixty minutes. No untoward effects occurred *In an occasional case there was a little pain* and tenderness, and in only 2 per cent of cases a small tender nodule developed which was absorbed The authors used the preparation in 115 cases with good results

More recently, Vorzimer and co-workers[41] reported the use of a concentrated aqueous solution of heparin, 200 milligrams per 1 cc. emulsified in 1 cc. of a mixture of cholesterol derivatives, peanut oil and beeswax. When given intramuscularly in doses of about 1 5 to 2 milligrams of heparin per pound of body weight, they obtained a prolonged coagulation time of 200 to 900 per cent of normal for seventeen to twenty-four hours. There were no toxic effects, no hemorrhage at the site of injection, and pain was negligible. This preparation has the advantage over that used by Stats and Neuhof of having a more prolonged action, and therefore, requiring less frequent injections.

Dicumarol has one advantage over heparin in that it can be used orally It has, however, some disadvantages In the first place its effect is delayed for one or two days after the use of the drug has been started. For this reason, if immediate anticoagulant effects are desired, this drug can not be used. Also, severe hemorrhage may occur in some cases, even after the drug has been discontinued. Another disadvantage is that it can not be safely administered without repeated laboratory determination of the

prothrombin time. This requires an experienced technician, and a uniform technic to be used in the same case all the time.

The usual procedure is to determine the prothrombin time of the patient each day by the Linke Shapiro dilution modification of the Quick method. This should be done before the drug is administered. The first day the patient receives 300 milligrams of dicumarol, the second day 200 milligrams, and this or smaller dosages are continued until the prothrombin time is reduced to about 20 per cent of normal The drug is then stopped, but the prothrombin time determination is continued daily or every other day thereafter As soon as the prothrombin time rises much above 30 per cent of normal the drug is given again in 100 or 200 milligram dosage, depending upon the percentage rise

Allen and co-workers[42] advise caution in the use of dicumarol or not to use it at all in renal insufficiency, after brain or spinal cord operation, in the various blood dyscrasias, in ulcerative lesions of the gastrointestinal tract, in nutritional deficiencies, in hepatic disease associated with prothrombin deficiency and in subacute bacterial endocarditis

Where anticoagulant therapy is urgent and its prolonged action is desired, it is advisable to start treatment with heparin and dicumarol at the same time—heparin for its immediate effect and dicumarol for its more prolonged action On the second or third day heparin may be discontinued and therapy may be continued by dicumarol alone.

Venous Ligation: As said before, in those cases where pulmonary embolization from venous thrombosis occurs repeatedly and is not controlled by anticoagulants, surgical ligation of the femoral vein of the affected leg may be advisable Where the source of embolization is in the pelvic veins, ligation of the inferior vena cava may be necessary Thebaut and Ward[43] feel that this should be done in preference to anticoagulant therapy where the patient shows evidence of repeated embolization Their mortality rate from the operation was very small

Ray and Burch[44] found no diminution in the functional capacity of the legs after the ligation of the inferior vena cava and there was no intermittent claudication Mild, to extreme edema followed operation, but cleared up within two months in most cases The large veins of the legs and feet were not dilated as a rule and no demonstrable varicosities were noted The superficial veins of the abdominal wall and gluteal region and the long thoracic veins were dilated.

REFERENCES

1 Cowdry, E. V, Editor Arteriosclerosis New York, The Macmillan Co, 1933
2 Hueper, E V Arteriosclerosis Arch Path 38 162, 1944, Ibid 38 245, 1944
3 Moschcowitz, E Vascular Sclerosis New York, Oxford U Press, 1942
4 Wilens, S L Bearing of general nutritional state on arteriosclerosis Arch Int Med 79 129, 1947

5 Joslin, E P Arteriosclerosis and diabetes Ann Clin Med. 5 1061, 1927

6 Leary, T Pathology of coronary sclerosis Am Heart J 10 328, 1935.

7 Winternitz, T, and LeCompte, P. M. The Biology of Arteriosclerosis Baltimore, C C Thomas, 1936.

8 Paterson, J C Vascularization and hemorrhage of the intima of arteriosclerotic coronary arteries Arch Path 22 313, 1936, Ibid 29 345, 1940

9 Knisely, M H, Bloch, E H, Eliot, T H, and Warner, L: Sludged blood Science 106.431, 1947

10 Monckeberg, J G Über die reine Mediaverkalkung der Extremitatenarterien und ihr Verhalten zur Arteriosklerose Virchows Arch f Path Anat 171 141, 1903

11 Freeman, N E, Leeds, F H, and Gardner, R E Sympathectomy for obliterative arterial disease Indications and contraindications Ann Surg 126 873, 1947

12 Nygaard, K K, and Brown, G E Essential thrombophilia Report of five cases Arch Int Med 50 82, 1937

13 Conner, L A A discussion of the role of arterial thrombosis in the visceral diseases of middle life, based upon analogies drawn from coronary thrombosis Am J M Sc 185 13, 1938

14 Buerger, L Circulatory Disturbances of the Extremities Philadelphia, W B Saunders Co, 1924

15 —— Thrombo-angiitis obliterans A study of the vascular lesions leading to presenile spontaneous gangrene Am J M Sc 136 567, 1908

16 Taub, N Mesenteric involvement in Buerger's disease J A M A 96 1469, 1931

17 Davis, L, and Ferret, G Cerebral thrombo angiitis obliterans Brit J Surg 34 307, 1947

18 Sigler, L H Study of thromboangiitis obliterans Ann Int Med 3.475, 1925

19 Schreiber, R Neber Polyarteritis Nodosa O Kümmel, Konigsberg, 1 Pr, 1904

20 Harris, A W, Lynch, G W, and O'Hare, J P Periarteritis nodosa Arch Int Med 113 1163, 1939

21 Diaz-Rivera, R S, and Miller, A J Periarteritis nodosa A clinicopathological analysis of seven cases Ann Int Med 24.420, 1946

22 Banowitch, M M, Polayes, S H, and Charet, R Periarteritis nodosa Report of five cases Ann Int Med 17 1149, 1942

23 Naide, M, and Sayen, A Venospasm—Its part in producing the clinical picture of Raynaud's disease Arch Int Med 77 16, 1946

24 Allen, E V, and Brown, G E Raynaud's disease A critical review of minimal requisites for diagnosis Am J M Sc 183 187, 1932

25 Carp, L Association of Raynaud's disease with cerebral symptoms Arch Surg 22.409, 1931

26 Duryee, A W, and Wright, I S The treatment of scleroderma by means of acetyl beta methyl choline chloride (mecholyl) iontophoresis Am Heart J 14 603, 1937

27 Kovacs, J The iontophoresis of acetyl-B-methycholine chloride in the treatment of *chronic arthritis and peripheral vascular disease: preliminary report* Am J M Sc 188 32, 1934

28 Lewis, T Vascular Disorders of the Limbs New York, Macmillan Company, 1936

29 White, J. C The Autonomic Nervous System New York, Macmillan Company, 1935

30 DeSansa, P A The innervation of the veins Its role in pain, venospasm and collateral circulation Surgery 10 731, 1946

31 [illegible] Thrombophlebitis: Role of vasospasm in the production [illegible] 117, 1940

32 [illegible] kers: Etiology and prevention of thrombosis of

[34] Neuhof, H · Venous thrombosis and peripheral pulmonary embolization J Mt Sinai Hosp 14·110, 1947.
[35] Kelsey, M P., and Comfort, M S Occlusion of the hepatic veins A review of twenty cases Arch Int Med. 75 175, 1945
[36] Baker, E C : Clinical and roentgenologic evaluation of venography Am J Roent 58·603, 1947
[37] Meyer, O · The ambulatory treatment of phlebitis, thrombophlebitis, and thrombosis with compression bandages. Surgery 21 843, 1947
[38] Allen, E. V.. The clinical use of anticoagulants Report of treatment with dicumarol in 1686 postoperative cases. J A M A. 134 323, 1947
[39] Loewe, L , Rosenblatt, P , and Hirsch, E Venous thromboembolic disease J A M A 130 386, 1946
[40] Stats, D , and Neuhof, H Concentrated aqueous heparin A new form of intramuscular administration Am J M Sc 214·159, 1947
[41] Vorzimer, J J , Sussman, L N , and Marder, M J · Prolongation of action of heparin J A M A 131·747, 1948
[42] Allen, E V , Hines, E A , Jr , Kvale, W F , and Baker, N. W.· The use of dicumarol as an anticoagulant Ann Int Med 27 371, 1947
[43] Thebaut, B R , and Ward, C S *Ligation of the inferior vena cava in thromboembolism* Surg , Gynec & Obst 84 386, 1947
[44] Ray, C T , and Burch, G Vascular responses in man to ligation of the inferior vena cava Arch Int Med 80 587, 1947

CHAPTER XX

Coronary Occlusion and Myocardial Infarction

IT HAS been shown in Chapter XIV that angina pectoris is considered to be a manifestation of transient coronary insufficiency. In the vast majority of cases, this occurs in coronary sclerosis However, the symptoms are not caused by the structural disease of the coronary vessels per se, but by the inability of those vessels to meet the demands of the myocardium for more blood supply under physical or mental activity. In other words, the symptoms are due to *functional inadequacy* of the coronary vessels.

In this chapter, we shall discuss the symptom-complex of coronary disease induced by *structural occlusion* of one or more of the coronary vessels, resulting in myocardial infarction We shall also include, in the discussion, occasional instances of coronary occlusion without myocardial infarction and myocardial infarction without evident occlusion

Historical Note

It is a very interesting and puzzling phenomenon in the progress of medicine, to find that a characteristic clinical entity such as that presented by coronary occlusion could have been overlooked until comparatively recent years Although the pathology of coronary thrombosis has been known for generations, its clinical manifestations were recognized for the first time by Obrastzow and Strachesko[1] in 1910 and were more fully identified and described by Herrick[2] in this country in 1912 The more puzzling fact is that the profession generally first began to diagnose the disease several years later when in 1919 Herrick[3] again called attention to its characteristic clinical manifestations. In that year, that author reported a case of coronary thrombosis in a man that he had diagnosed during life The report was accompanied by electrocardiographic findings, and the diagnosis was proved by autopsy Since then, there has been rapid development of our knowledge of the clinical and electrocardiographic changes of the disease, as described elsewhere.[4]

Incidence

The incidence of coronary thrombosis is not definitely known. Some idea of its prevalence may be gathered from Vital Statistics, Special Reports[5] covering the year 1944. In that year alone, 124,493 deaths were due to coronary disease and angina pectoris in the United States, representing a total of 93 9 per 100,000 of the population. Although coronary thrombosis is not specifically mentioned, from clinical experience, we know that up-

wards of 70 per cent of coronary deaths are due directly, or indirectly to coronary thrombosis This would make a total of at least 87,145 deaths due to coronary thrombosis in that year. Inasmuch as the estimated mortality rate is about 15 per cent that of the morbidity rate, as shown in Chapter I, the estimated number of persons suffering from the disease in that year was at least 600,000 This undoubtedly is greatly underestimated, for many of the 268,030 deaths due to other forms of heart disease were undoubtedly those of coronary thrombosis. Master[6] estimated that about 800,000 suffered from the disease in 1942.

Like other forms of heart disease, coronary thrombosis has shown a progressive increase in mortality and morbidity within the past three decades, since its recognition as a clinical entity. Although the tremendous number of cases observed in recent years may partly be due to a more frequent recognition of the disease, it appears to be due mainly to an actual increase in the number of cases.

The condition is more prevalent among males than females, the incidence being approximately 3:1, and men experience the first attack, on the average, about four years earlier than women. There appears to have been, however, an increase in the frequency and in the incidence of the earlier onset of the disease among women in recent years.

The first attack of coronary thrombosis is observed most frequently between 50 and 70 years of age, and its frequency diminishes moderately between 40 and 50 years. Below 40 years of age, the incidence diminishes progressively, the greatest diminution occurring below 30 years of age, and it is comparatively rare below 20 years of age The youngest case treated by the author was a 19 year old male

The incidence of coronary disease in individuals younger than 40 years of age appears to be much more frequent than we have previously considered it to be This is shown in the recent interesting report on 866 cases of its occurrence in individuals 18 to 39 years old in the armed services in World War II, submitted by Yater and co-workers.[7] In this series there were 8 cases, 20 years old or younger, 247 between 21 and 30 years, the rest were 31 to 39 years old. They also quote 744 cases of coronary disease reported in the literature on individuals in the same age groups. Among these were 14 below 20 years of age, 128, 20 to 29 years, and the rest between 30 and 39 years old

Stryker[8] reported 9 cases of coronary occlusion in infants and children under 17 years of age. However, the underlying pathology in such cases is not coronary sclerosis, but localized inflammation of the arterial wall due to any cause or to atheromatosis, embolization from some source or some congenital abnormalities. Ravitch and Rosenblatt[9] have recently reported two cases of myocardial infarction in two infants, 2 days, and 10½

hours of age respectively The underlying cause here could not be definitely ascertained. There appears to be a somewhat greater incidence of attacks of coronary thrombosis in the winter and spring than in the summer and fall, according to various reported series This has also been the author's experience Brown and Pearson[10] found the death rate from coronary disease in New York City to be 24 2 per cent greater in December than in August, and for all types of heart disease 18.8 per cent greater

Etiology

The underlying fundamental cause of coronary occlusion is, in the vast majority of cases, coronary sclerosis and atheromatosis In rare cases, syphilis, periarteritis nodosa, thromboangiitis obliterans or other conditions affecting the coronary vessels mentioned above may be the background for an occlusive process In very rare instances, an occlusive process may result from an embolus The etiology of coronary occlusion is primarily, therefore, the etiology of arterial disease, discussed in Chapter XIX

The precipitating causes of coronary occlusion are not known. In most cases, the attack comes on apparently spontaneously, without any evident cause In fact, in a great many cases, the attack occurs while at perfect rest, or during sleep In some cases, however, an attack may follow *immediately or soon after unusual physical exertion, mental strain,* emotional upset, exposure to extreme cold, a heavy meal, an operation, some infection, alcoholic excesses, or other departures from the usual and accustomed life of the individual

There is a great deal of controversy in the literature as to whether or not any one of these factors is actually responsible for the attack, or is merely a coincidental condition Master[11] believes that these factors are merely coincidental. He found that in only 2 per cent of his cases was an attack preceded by unusual exertion, and in 5 per cent by excitement. Mintz and Katz,[12] in examining the records of 474 cases, likewise, found only 9 5 per cent of cases in which there was some factor present in each case which might be considered a precipitating cause. They felt, however, that inasmuch as they personally did not question the patients directly, but received their information from records, they cannot rely on the data

In hundreds of cases where the author personally obtained the history of the circumstances under which the attack occurred, he found that 80 per cent had no evident provocative cause In the remaining 20 per cent, however, there were some factors which could be considered provocative. In some, the attack occurred during strenuous play For instance, a woman, 30 years of age, who never had had any complaints, was playing a game of handball while on her vacation. After ten minutes of continuous play, she developed an attack which proved to be acute coronary occlusion resulting in posterior left ventricular wall infarction.

Occasionally, the attack occurs during or immediately after sexual relations. For example, a male, 45 years old, who presented a mild form [illegible] widespread coronary sclerosis and a fresh thrombosis of the anterior descending branch of the left coronary artery.

The author has cases on record where the attack followed immediately or occurred during an exciting argument, a competitive card game, a ball game, overeating, cranking a car, mowing a lawn, or in the course of physical work in connection with the usual occupation of the patient.

In some cases, there were two or more factors that appeared to have played a part. For instance, a man, 40 years old, who was subject to "digestive disturbances" for several years had severe aggravation in his business one morning which gave him some precordial discomfort. In an attempt to overcome the uncomfortable feeling, he partook of a very heavy meal Soon after the meal, he developed excruciating precordial pain, radiating to both arms and collapsed. The subsequent course was that of acute myocardial infarction affecting the anterior wall of the left ventricle.

In some cases who were subjected to extreme physical strain, the attack developed within one or more hours after such strain. In most of these, a certain amount of discomfort was experienced during the strain or soon after, then became progressively worse, finally culminating into a major acute attack. For example, a male electrician, 35 years old, had to pull a heavy cable through a metal tubing under great resistance, a distance of about 150 feet He experienced sharp precordial pain which soon subsided, leaving a dull ache He continued working and experienced marked weakness so that he had to sit down and rest He then had his dinner, following which he had an uncomfortable feeling. Five hours later, he developed a severe "spontaneous" attack while at rest in bed It lasted several hours, and resulted in acute anterior left ventricular wall infarction.

In occasional cases, some discomfort was felt during the strain, but subsided entirely for some time only to return again during the day and to be followed by a major attack which developed in the middle of the night. In still others, there was no discomfort during the strain and the attack developed a little later. For example, a male, 39 years old, whose car stalled, was compelled to push it a distance of about 50 feet. He did not experience any discomfort while pushing, but after having driven for about one hour, he developed a severe attack which proved to be that of posterior left ventricular wall infarction.

There have also been some instances where major attacks of coronary

occlusion occurred one or more weeks after unusual physical or mental strain or emotional upset. Previously, the patient was asymptomatic and following the strain, there was either mild recurring pain or a continuous dull ache, appearing on the slightest exertion or spontaneously. We must assume that in such cases, something has happened in the coronary system during the original strain which produced the anginal syndrome culminating finally in a major branch occlusion and myocardial infarction In some of these cases, only a careful inquiry brought out the fact that the original onset of the condition followed the unusual strain or emotional disturbances Many of the patients forget the circumstances that apparently precipitated the attacks

In some cases, the attack developed soon after a heavy meal or several hours later If later, the patient usually felt considerable discomfort soon after partaking of the meal, especially so if he attempted to walk or if excited The culmination was an acute episode which occurred several hours later, at rest. One case developed an attack immediately after drinking a glass of ice water

Attacks occasionally follow prolonged overindulgence in food and liquor. For example, a healthy male, 44 years old, who hever had any complaints referable to his heart, took a trip to Europe. On the fifth day of excessive drinking, eating and "having the grandest time of his life" in cabarets on the continent, he suddenly developed severe retrosternal pain radiating to the epigastrium, neck, face and jaws, lasting ten hours. It recurred in milder form on the following day, lasting about eighteen hours. Evidently, the condition was overlooked by the examining physician, for he was allowed to travel back to this country He felt rather tired and "sickly" on his trip back home, and so he rested more or less on board ship On arrival, examination revealed an acute posterior left ventricular wall infarction.

These experiences leave no doubt that in many cases the factors cited are more than coincidental and must be considered provocative. The author agrees with Fitzhugh and Hamilton,[13] Boas,[14] Blumgart[15] and others who hold a similar view

Pathology and Pathogenesis

Occlusion of a coronary vessel is dependent upon two main pathologic changes. One is the occurrence of marked thickening and increased vascularity of the intima and the other, the development of degenerative changes in the form of atheromatous plaques

As a result of increased vascularity of the intima, intramural hemorrhages develop in the arterial wall, as has been shown by many observers in the past, and has been recently stressed by Paterson,[16] Leary,[17] and Wartman.[18] These intramural hemorrhages, by their accumulation of

blood in the vessel wall, produce bulging of the intima and narrowing of the lumen. They also stimulate more degeneration of an overlying atheromatous plaque, resulting in an "atheromatous abscess" which may rupture into the lumen. In many cases, the deposition of a thrombus on the surface of the plaque may occur. Such a thrombus may produce occlusion at the site or may be removed by the coronary blood stream and carried forward to plug a branch of the vessel further down. In this respect, the thrombus serves as an embolus.

In 100 cases of coronary occlusion studied by Horn and Finkelstein,[19] 62.5 per cent had their origin in intramural hemorrhage and 37.5 per cent in the formation of a thrombus on an arteriosclerotic plaque. They point out that there is coexistence of recent and organizing changes within a plaque or its thrombus which indicate that coronary occlusion may be a slow and progressive process.

With these slowly progressing pathologic changes that precede the final complete occlusion of a coronary vessel, we can understand why a great many cases show premonitory symptoms for hours, days or weeks before an acute episode. We can also understand how the pathologic processes leading to complete occlusion may be precipitated or expedited by physical or mental strain, and other conditions enumerated above, long before the acute episode of final complete occlusion occurs.

An occlusion of a coronary vessel results, in most cases, in infarction of that portion of the heart muscle which derives its main blood supply from the given vessel. The infarcted area is irregular in shape, of yellowish or white appearance, and is frequently surrounded by an area of congestion. It is usually firm in consistency, but when large, it may break down into a granular mass. Accumulation of blood may occur in its substance, resulting in a deep red color. Softening of a myocardial infarct is known as *myomalacia cordis*, and if it occurs in a large area, it may lead to a rupture of the heart. In the vast majority of cases, however, the infarcted area ultimately becomes replaced by fibrosis. When the replacement fibrosis is complete the process is spoken of as an *organized or healed infarct*. If the scar is large, an aneurysm may develop in that area as a result of intraventricular pressure.

An infarct may vary in size from less than one half to more than 10 centimeters. Depending upon the size of the infarct and its location in relation to the pericardium or endocardium, it may lead to mechanical or aseptic pericarditis or endocarditis. In the latter condition, mural thrombi may develop at the site of the endocardial involvement which may serve as emboli.

In most cases, infarction of the heart occurs in the anterior and apical portion of the left ventricle due to closure of the anterior descending branch of the left coronary artery. In many cases, they occur in the posterior

wall or in the median portion, due to occlusion of the right coronary or circumflex branch of the left coronary artery. Multiple infarctions occur frequently. Infarction of the right ventricle is comparatively rare.

Infarction involving the interventricular septum may result in rare cases, in perforation of the septum

Microscopically, the infarcted area, shows acute destructive changes of the muscle cells in stages varying from loss of striation, swelling, granulation of the cytoplasm to their complete disappearance. Leukocytic and



Fig 96—Acute Myocardial Infarction An area of the heart adjacent to that shown in Fig 97 Many of the heart muscle fibers show various degrees of destructive changes Marked arteriolar and capillary distention with blood and some hemorrhage are noted × 80

hemorrhagic infiltration of the necrotic tissue takes place. This is illustrated in Figure 96. In the later phases, the area becomes replaced by fibroblasts and soft granulation tissue with numerous small blood vessels, as shown in Figure 97 This eventually is converted into dense fibrous ... seen in the same case

... ly occurs as a result of infarction, it may also occur as a slowly developing process in the course of progressive coronary insufficiency. Hence, the finding of myocardial

fibrosis at autopsy does not always indicate that acute coronary occlusion had occurred at one time or another during life Myocardial fibrosis may also result in occasional cases from rheumatic myocardial involvement and other conditions without gross coronary sclerosis, as shown by Brown [20]

Inasmuch as myocardial infarction is the result of an acute shutting off of the blood supply to a given portion of the heart, its development is dependent upon the size of the vessel occluded, the rapidity of occlusion and the extent of the collateral circulation For infarction to occur, the oc-



FIG 97—MYOCARDIAL INFARCTION Area where the muscle fibers have completely disappeared and are replaced by fibroblasts and soft granulation tissue Several small blood vessels are noted which are markedly distended with blood. × 80

cluded vessel must be of considerable size and the collateral circulation must be poorly developed If the occluded vessel is of a small caliber and if the collateral circulation is good, no infarction will occur. In such cases, the symptoms of occlusion may develop without the subsequent clinical and electrocardiographic evidence of infarction Also, the occlusion must be acute Slowly developing occlusions may result in the establishment of a sufficient collateral circulation to prevent infarction.

In a study of 166 hearts by the Schlesinger injection method, Ravin and Geever[21] demonstrated that the balance between the rate of narrowing

of the coronary arteries by sclerosis and occlusion and the development of a colateral anastomosis will decide what happens to the myocardium. The longer the occlusion is delayed by rest and vasodilators, the better chances for a collateral circulation to develop and for infarction to be prevented These factors are important from a diagnostic, therapeutic and medicolegal viewpoint

In cases where coronary disease is extensive or where prolonged myocardial ischemia occurs for various reasons, myocardial infarction may occur without acute coronary thrombosis or occlusion, as was shown by Schlesinger,[22] Gross and Sternberg,[23] Friedberg and Horn[24] and other investigators In such cases, prolonged disturbances in the dynamics of the coronary circulation are contributing causes of infarction. The mechanism of such disturbances is not definitely known and probably varies in different cases According to Gross and Sternberg, some of the possible mechanisms are dependent upon mechanical, reflex and humoral factors. The mechanical factors may consist of a temporary fall in intra-aortic pressure, extreme tachycardia and cardiac hypertrophy Reflex factors producing prolonged vasoconstriction may originate in the heart itself or in other parts of the body, especially the gastro-intestinal tract or in the brain Humoral factors may consist of adrenalin, histamine and vasopressor substances of the posterior pituitary gland

These considerations demonstrate the complexity of the problems of the pathogenesis of coronary occlusion and myocardial infarction Although the structural pathology of the disease is well known, the functional pathology is not as yet fully understood There may be a great many other constitutional or humoral factors which enter into the production of the disease, such for instance as smudging of blood, the accumulation of lactic acid or other products of metabolism in the heart and so on Recently, Govier[25] has shown that there is a destruction of intracellular co-enzymes in heart muscle rendered ischemic by coronary ligation He suggests the use of nicotinamide, riboflavin and succinate to help prevent such destruction

Clinical Manifestations

The usual mode of onset of coronary occlusion is very dramatic and cannot escape the attention of the observer The patient suddenly experiences severe agonizing precordial or retrosternal pain or a sense of oppression, constriction or strangulation, associated with shock. A cold clammy perspiration covers his entire body. There is marked pallor or ashen color, the pulse may become weak or even imperceptible and the blood pressure drops. These symptoms are followed within twenty-four to forty-eight hours by a rise in body temperature, leukocytosis and increased sedimentation rate of the blood cells. In many of the serious cases, abnormali-

ties in the character and in the intensity of the heart sounds occur A gallop rhythm often develops and in some cases a pericardial friction rub may be heard.

Although this symptom complex of coronary occlusion seems to appear spontaneously, a great many patients have prodromal symptoms heralding the attack, as said before. Also in about 70 per cent of cases, the anginal syndrome has preceded the attack by days, weeks, months or years.

We shall attempt to present here the manifestations of the disease in more detail, setting forth the variations from the usual train of phenomena, often observed.

Prodromes: Although the occurrence of the anginal syndrome may be considered a warning sign that sooner or later an attack of coronary occlusion may occur, it is not a true prodromal manifestation When, however, the anginal syndrome which has been running true to form for a long time suddenly changes its character, becoming very severe, more prolonged and occurring spontaneously, it is to be considered an immediate forerunner of acute coronary occlusion. This is also true if angina was not present before, but suddenly appears for the first time in a very severe form and recurs frequently For example, a male, 47 years old, who never had any complaints before, developed severe pain in the neck, radiating to the midsternum, while walking, lasting eight minutes This recurred two days later on walking and after meals. In the middle of the night, on the third day, he was awakened by a very severe attack, lasting all night, which was followed by anterior left ventricular wall infarction

In those cases where these short spontaneous seizures are followed by longer ones, progressive recurring occlusive changes of the smaller branches of the coronary tree are undoubtedly taking place. This is corroborated by pathologic reports of various observers where usually more than one coronary vessel is found occluded in the same heart

A good example is a male, first seen when he was 32 years old. For three years previously, he was subject to short recurring sensations in the precordium, described by him as "needle-prick like pains," and nine months before observation he had an episode of severe pain in the left nipple region while playing golf, lasting two seconds. He was able to finish the game, however, without further discomfort. Following that, he had slight shortness of breath on climbing a few stairsteps for about ten days. During the night, on the tenth day, he was awakened from sleep by severe pain extending from the left nipple to the left shoulder, lasting fifteen minutes, associated with cold perspiration. This recurred 4 times during that night. It was associated with frequent bowel movements which he had experienced on any excitement for many years. His temperature rose the

following day to 100 5 degrees F. and the electrocardiogram showed evidence of infarction of the posterior left ventricular wall Subsequently, he was subject to recurring attacks of nausea and right precordial pain on exertion, associated with belching and heartburn. He was an extremely nervous individual and symptoms were more apt to occur when he worried, or on excitement From time to time over a period of five years, while under observation, he had spontaneous attacks of precordial pain varying in duration from five minutes to several hours, most of which were mild He died suddenly at 37 years of age, after a severe attack lasting two hours Autopsy revealed a marked degree of coronary sclerosis with several areas of old occlusions and myocardial fibrosis as well as some areas of more recent occlusions and a fresh thrombus in the main stem of the anterior descending branch of the left coronary artery

In some cases, the prodromes may be in the form of severe exhaustion, marked "gaseous disturbances," transient dizziness, and various other abnormalities rather than pain. In many such cases, only a careful inquiry into the subjective sensations of the patient before the major attack of coronary occlusion will reveal that prodrome symptoms existed before the major attack

Subjective Manifestations The most frequent manifestations are severe agonizing, constricting precordial pain and a sense of suffocation The pain may radiate in various directions, as described under angina pectoris, in Chapter XIV In coronary occlusion, however, the symptoms are far more severe, last much longer and the area of radiation may be wider Some of the descriptions of the pain given by various patients are, burning, griping, squeezing, pressing, choking, heaviness, cramplike, smothering, crushing, knifelike, tightening and shooting The duration of these acute, subjective sensations may be from fifteen minutes to several days The usual duration is two to six hours The onset is usually abrupt but it may be gradual, extending in a mild form for one or more days until it becomes very severe During this period of milder pain, it is accentuated by strain and excitement, as described under prodromes

In some cases, the location of the pain or other sensations may be atypical. Thus, it may occur in various parts of the head, neck, one or both arms, right side of the chest or in the back of the chest, especially in the left scapular region *Occasionally, the pain may be referred to the lower* chest or upper abdomen and may be associated with moderate abdominal rigidity and some tenderness which together with shock and vomiting may be mistaken for an acute surgical abdominal condition. The pain is usually continuous but may be intermittent

Occasionally, instead of pain, the patient may describe his sensation as "acute indigestion" with severe bloating, gaseous eructation and "heart-

burn" In other cases, the onset of the attack is by syncope. This is true especially if the auriculo-ventricular conduction apparatus is involved, resulting in transient auriculo-ventricular block but it may also occur in the absence of such involvement In such cases, there may be no precordial pain or merely a little discomfort. In 100 cases of coronary occlusion that came to autopsy, Race and Lisa[28] found that 5 per cent had their onset with cerebral manifestations but showed no brain pathology In 15 per cent, there were vascular accidents of the brain in addition to myocardial infarction.

In some cases, the onset may be in the form of marked dyspnea and pulmonary edema. This is more apt to occur in the advanced form of arteriosclerotic heart disease In occasional cases, there may be no symptoms associated with myocardial infarction This is true especially in elderly individuals with advanced congestive failure or in severe debilitating disease, particularly in cerebral arteriosclerosis with encephalomalacia where the sensorium is very poor. In occasional cases, the onset of the attack may be in the form of extreme exhaustion and collapse, associated with marked restlessness and fear of impending death. Some of these cases also have a peculiar, indescribable feeling of choking

Objective Findings. The ashen color and cold, clammy perspiration frequently occurring at the onset, usually subside with the disappearance of the acute symptoms. In severe cases, however, they may persist longer and in early fatal cases, until death

The *quality of the pulse* and the *height of the blood pressure* vary with the severity of the disease In mild cases, no alterations occur early. In fact, in occasional cases, the blood pressure may even rise temporarily. In severe cases, the pulse is weak or may become imperceptible and the blood pressure drops correspondingly. The weak pulse and the drop in pressure may persist long after the other symptoms of shock subside

The underlying cause of the weak pulse and drop in pressure is probably some degree of forward failure of the left ventricle as suggested by Mendlowitz and co-workers[27] It may partly be due also to products of absorption from the infarct which act on the arteriolo-capillary bed, producing some degree of peripheral vascular failure. If hypertension existed before the coronary occlusion, a normal blood pressure reading after the attack indicates, of course, a drop in pressure.

The fall in blood [illegible]

both [illegible]

sure [illegible]

pressure The maximum drop usually occurs within twenty-four hours after the attack, although in some cases, there is a gradual drop reaching the lowest levels by the end of one or two weeks. A persistent systolic

level of 80 mm or less and a pulse pressure of less than 25 mm carry a poor prognosis

The heart rate and rhythm may be normal in mild cases, although an occasional premature contraction may occur. In severe cases, there is usually an acceleration of the heart rate, reaching, at times, as high as 120 or more per minute In occasional cases, auricular or ventricular paroxysmal tachycardia, auricular flutter or fibrillation develop In such cases, the ventricular rate may be as high as 180 or more per minute. In some cases, the rate is slow due to sinus bradycardia, or auriculo-ventricular block If sinus bradycardia occurs it is often associated with sinus arrhythmia If auriculo-ventricular block is present there may be a marked irregularity due to dropped ventricular beats In rare cases of sinoauricular standstill or auriculo-ventricular block with ventricular asystole, the Adams-Stokes syndrome may occur at the onset or in the course of the disease The author reported examples of the latter[28] and complete reviews of the subject are found in the reports by Schwartz[29] and by Master and co-workers[30]

The *heart sounds* in the milder cases and even in some severe cases, may show no significant changes In very severe cases, the first sound may become very weak, muffled or shortened and there may be an admixture of a faint murmur. The second sound, likewise, becomes weaker than normal and the pulmonic often becomes greater than the aortic second sound. A gallop rhythm frequently occurs in severe cases.

The sudden onset of a rough, loud systolic murmur in the fourth and fifth left interspaces close to the sternum speaks for perforation of the interventricular septum due to infarction in that region. Such perforation is usually associated with recurrence of sudden pain in the precordium and congestive failure Wood[31] collected 38 cases from the literature. I have observed one case in which the diagnosis was confirmed by autopsy.

A *pericardial friction rub* occurs in about 10 per cent of cases of coronary occlusion It may be faint and strictly localized or rough and widespread It should be looked for frequently as its occurrence is a very good diagnostic sign. In some cases, it may appear within a few hours after the onset, in others, it may not be heard till the end of the first week It is most often heard between the second and sixth days. It may last a few hours to several days

The temperature is an excellent index in most cases of the amount of myocardial infarction It usually appears within twenty hours of the onset of the disease, but in some cases, it appears within one or two days. In mild involvement, it may not rise to more than 100° F. and it remains elevated one or two days. In more severe cases, it may rise to 102° F. or slightly higher and gradually diminishes, coming down to normal in three to six days. In very severe cases, the initial rise may be as high as

103° or more and may slowly abate over a period of two or more weeks In such cases, we must always look for some additional complicating factor that might account for such rise If fluctuating, it may indicate recurring progressive myocardial infarction, or embolization to various parts of the body with secondary infarction These usually present other signs by which the diagnosis can be established

The temperature should always be taken by rectum A mouth temperature is unreliable In fact, due to the presence of shock, the mouth temperature may at times be subnormal while the rectal temperature is elevated above normal. It is also important to determine the temperature three or four times a day If determined less frequently, it may be overlooked, especially in mild cases

Meteorism or abdominal distention is at times an extremely troublesome condition It occurs most often in severe cases and is probably due to some degree of paralytic ileus It is usually associated with belching and at times with hiccough It often results in great embarrassment of respiration and increases the disturbances in the circulation. Hiccough may occasionally occur in myocardial infarction in the absence of abdominal distention

Congestion of the lungs at the bases is almost always present and in severe cases, widespread pulmonary edema may be evident.

Laboratory Findings

The leukocyte count occasionally begins to rise within a few hours after the onset of the disease, although the maximum rise may appear after two or three days The count may vary between 10,000 and 16,000 cells per cubic millimeter, although in some cases, it may be higher, approaching 30,000 in very rare cases When the higher figures are obtained, however, we must look for complications The number of polymorphonuclear cells is relatively increased. In some cases, the white blood cell count may remain within normal limits throughout the disease In occasional cases, an increase in the white cell count may occur in the absence of a rise in temperature

The blood cell sedimentation rate is accelerated and in some cases, markedly so It often is a better index of the amount of activity than the white cell count and temperature Many cases showing a normal white cell count or normal temperature may have an accelerated sedimentation rate In some cases, however, the sedimentation rate may remain normal or only slightly accelerated where the clinical findings definitely point to the presence of myocardial infarction We often find also that the sedimentation rate remains elevated six to ten weeks or longer after the onset of the disease when all signs point to the absence of active myocardial changes In such cases, the accelerated rate may be due to a

possible focus of infection or other factors, and not to myocardial infarction

The blood sugar is usually elevated soon after the onset of coronary occlusion and may remain so for several days The level may, in rare cases, reach as high as 250 milligrams or even more per 100 cc. of blood. A certain number of cases show also a low grade glycosuria and occasionally acetonuria. These facts must be borne in mind so as not to consider the case one of diabetes.

The blood urea nitrogen may also show abnormally high figures in a small number of cases, after the attack and return to normal in a few days

The underlying causes of the elevation of the blood sugar and urea nitrogen are not known. It may possibly be due to transient circulatory disturbances of the pancreas and the kidneys respectively caused by capillary stasis, or by diminished cardiac output which results in functional insufficiency of those organs. It may also be due to autonomic nervous system disturbances including the controlling centers in the hypothalamic region of the brain.

Differential Diagnosis

There are a great many diseased states which may simulate coronary occlusion As in the latter, shock may be the dominating feature in these diseases in the early phase, hence the difficulty in diagnosis in many instances The most important of these are acute abdominal, mediastinal, pulmonary, and aortic disease, acute pericarditis and radiculitis.

Acute Abdominal Disease: The more common forms of acute abdominal disease that may simulate coronary occlusion are acute cholecystitis and cholelithiasis, perforated gastric ulcer, and acute pancreatitis. Acute appendicitis and intestinal obstruction may also, in rare cases, be mistaken for coronary occlusion

Although the onset of an acute coronary occlusion, where there is a predominance of abdominal symptoms, may resemble that of acute abdominal disease, the differentiation is often not difficult In acute abdominal disease, the localization of the symptoms and signs are predominantly in the abdomen, while in coronary occlusion, they are usually referred predominantly to the chest Also, the mode of onset has some finer differences in the two conditions

The following are important differential points in the diagnosis of the more common acute abdominal conditions:

In *acute cholecystitis*, the onset is usually characterized by chills and fever, marked abdominal distress followed often by some jaundice. These symptoms together with the right upper abdominal pain, tenderness and rigidity are very seldom duplicated by coronary occlusion.

In *acute biliary colic*, there is no shock and the pain, tenderness, and rigidity are localized to the gallbladder region with radiation, if any, to the right shoulder Trapezius tenderness is often present.

In *perforated gastric ulcer*, the abdominal pain is excruciating and there is boardlike rigidity of the abdominal wall in the early stages, followed later by generalized abdominal pain and tenderness caused by peritoneal irritation. Due to escape of air into the peritoneal cavity, pneumoperitoneum may be demonstrated by x-ray

In *acute pancreatitis*, the onset of the pain is sudden. It is most intense in the mid-upper abdomen and it radiates to the back Early abdominal distention is often present and signs of peritonitis from fat necrosis are evident In doubtful cases, an elevation of serum amylase may help in the diagnosis

Acute Pulmonary Disease: The more common forms of acute pulmonary disease that may simulate coronary occlusion at its onset, are pulmonary embolization with infarction, spontaneous pneumothorax, sudden bronchial obstruction with pulmonary atelectasis, spontaneous interstitial emphysema and acute lobar pneumonia. Although the abruptness of onset of these conditions and the shock may be similar to those of coronary occlusion, careful physical examination of the lungs should offer no difficulty in arriving at a differential diagnosis This is especially true a day or two after the onset when the pulmonary findings are often unmistakable. The following are some points which may help in the differential diagnosis:

In *pulmonary embolization*, there is, as a rule, a sense of suffocation rather than precordial pain Chest pain, when present, is usually localized in other than the precordial region. It often occurs later in the course of the disease and is caused by pleural involvement over the infarcted lung area, if the infarction extends to the pleural surface The pain is therefore usually provoked by respiration Hemoptysis may be present The condition has been described in Chapter XVIII

Spontaneous pneumothorax is also usually characterized by a feeling of suffocation rather than pain and may be confused with the comparatively infrequent painless form of coronary thrombosis where dyspnea may be an outstanding feature The physical findings of tympanitic resonance, diminished expansion of the affected side of the chest and almost absent breath sounds on that side makes the differential diagnosis easy. A roentgenologic examination, Figure 98, confirms the diagnosis

Acute pulmonary atelectasis due to sudden bronchial obstruction is likewise characterized by marked dyspnea rather than pain, although considerable pain may be present over the affected side. The author recalls seeing a case of sudden bronchial obstruction in the course of bronchogenic carcinoma which was being treated for acute coronary occlusion The

physical findings of some displacement of the mediastinum and heart towards the affected side, diminished movement af the chest on that side, absent breath sounds over the involved area and the x-ray findings helped establish the diagnosis

Spontaneous interstitial emphysema may easily be mistaken for coronary occlusion It is characterized by severe precordial pain radiating to the

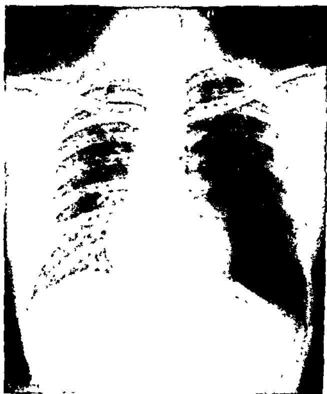


FIG 98—FROM A MALE, 25 YEARS OLD, WHO EXPERIENCED SUDDEN ONSET OF SEVERE PRECORDIAL PAIN AND A SENSATION OF PRESSURE RADIATING TO THE BACK OF THE CHEST [illegible]

left shoulder and arm, followed by a rapid pulse, low grade fever and leukocytosis, as in coronary thrombosis The pathology consists of rupture of an air sac and the dissection of the escaping air along the bronchi and blood vessels finally reaching and infiltrating the mediastinum. It may even reach the neck producing subcutaneous emphysema. It may also reach the pleural cavity producing pneumothorax. The most important differential point in the diagnosis is the peculiar crackling, crunching sounds syn-

chronous with the heart beat, described in Chapter VIII. The physical and x-ray findings of pneumothorax and x-ray evidence of the presence of air in the anterior mediastinum confirm the diagnosis.

Pneumonia may occasionally be mistaken at its onset and early course for coronary occlusion. In most cases, however, it should not be difficult to differentiate the two The onset with chill, early high rise in temperature and pain not being localized to the usual conventional areas seen in coronary occlusion should offer no difficulty in early diagnosis Later, the pulmonary findings are of course, sufficient to confirm the diagnosis.

Aortic Disease. Of the acute affections of the aorta that may be mistaken for coronary occlusion, the most important are rupture and dissecting aneurysm.

Rupture of the aorta, if incomplete, may or may not be followed by dissection. It usually occurs close to the commissure of the aortic valve. The symptoms may resemble coronary occlusion. The development of aortic insufficiency and the absence of electrocardiographic changes of coronary occlusion speak in favor of the diagnosis Rupture of the aortic valve may also produce the same symptoms.

In *dissecting aneurysms* of the aorta, the pain is much more excruciating than in coronary occlusion. A pre-existing hypertension which is frequently present, persists after the attack Depending upon the location and spread of the dissection, occlusion of the various branches springing from the aorta may take place resulting in corresponding signs and symptoms The subject is fully discussed in Chapter XXI

Acute Pericarditis: Acute inflammation of the pericardium may occasionally simulate myocardial infarction The pain in pericarditis, however, is never as marked and has not the usual character of coronary occlusion. The subject of pericarditis is fully discussed in Chapter XXV

Radiculitis: Recently Davis[32] called attention to spinal nerve root pain which may closely simulate that of coronary occlusion The pain is often confined to the substernal or precordial region, and radiates to the same areas as in coronary occlusion It may also be associated with pallor and perspiration. The distinguishing characteristics are that the pain usually occurs after certain movements of the spine such as bending or turning of the body, after coughing, sneezing, straining at stool or prolonged sitting. The attack may be reproduced by the application of pressure to the dorsal spine There may be some spasm of the posterior cervical muscles and tenderness at the costochondral junctions of the ribs and sternum. The condition may be benefited by postural correction, exercise, manipulation and traction of the cervico-dorsal spine.

The *most important single aid in the diagnosis of coronary occlusion* is

the electrocardiogram. A complete discussion of the electrocardiographic diagnosis of myocardial infarction is given elsewhere.[4]

Complications

The most common complication of coronary occlusion is embolization from mural thrombi in the affected ventricle According to Blumer,[33] 50 per cent of cases of coronary occlusion have mural thrombi and about 14 per cent present embolic manifestations. Embolization occurs most frequently in the lungs, but is also observed in any of the systemic arteries as in the brain, kidneys, spleen, mesenteric vessels, and extremities. It most often occurs within the first ten days, but the author has observed it in some cases as late as three weeks after the onset of infarction and in severe cases, later

The outcome of the embolic phenomena depends upon the size of the embolus Encephalomalacia and various forms of palsies, gangrene of the lower extremities, intestinal gangrene and pulmonary infarction may result, the last being most frequent. Eppinger and Kennedy[34] found pulmonary embolism to be the main or contributing cause of death in one quarter to one third of cases dying from coronary occlusion

Other important complications of myocardial infarction are venous thrombosis of the lower extremities and arterial thrombosis in other parts of the body, especially of the cerebral and coronary arteries. Venous thrombosis often results in pulmonary embolization The underlying causes are probably the prolonged bed rest resulting in added slowing of the circulation, and the effect of the products of absorption from the myocardial infarction. May and Barnes[35] found an incidence of 37 cases of embolic or thrombotic vascular accidents in 100 consecutive cases of coronary occlusion during convalescence Seven of these were in the nature of thrombophlebitis and 8 of cerebral artery thrombosis or embolization. Eighty-seven per cent of the vascular accidents occurred between the fourth and twentieth day

Secondary infections as a result of lowered resistance may occur as complications of myocardial infarction.

More direct complications of myocardial infarction often observed are the various arrhythmias, and different grades of heart block as well as heart failure. In an occasional case, rupture of the interventricular septum, mentioned before, and rupture of the wall of the affected ventricle may occur Both of these, especially the latter, are usually fatal. Among 270 cases of myocardial infarction, Friedman and White[36] found ten cases of rupture of the heart, on autopsy.

Prognosis

The immediate outcome of an attack of acute coronary occlusion depends upon the severity of the attack and the complications that develop. Mild

attacks with very little temperature or leukocytic reaction and no marked acceleration of the sedimentation rate, usually all recover. In moderately severe cases, the immediate mortality rate is about 5 per cent to 10 per cent. In extremely severe cases, the mortality rate may reach 50 per cent or higher. In 172 cases who showed severe initial clinical manifestations, Conner and Holt[37] found about one third recovered The over-all immediate mortality rate varies between 15 per cent and 25 per cent in the various reported series In the author's experience, the average immediate mortality is close to the lower figure

The factors that speak for a poor prognosis are prolonged and high elevation in the temperature with fluctuations; a persistently low blood pressure of 80 systolic or less, with other signs of prolonged shock; the occurrence and persistence of auricular fibrillation and paroxysmal tachycardia; the presence of marked and prolonged meteorism; and the occurrence of repeated embolic phenomena A widespread and loud pericardial friction rub, the frequent waning and waxing of the pulse, a persistently high grade simple sinus tachycardia with a gallop rhythm, and evidence of marked left heart failure likewise, carry a poor prognosis However, no case of coronary occlusion, no matter how serious it may appear, should be considered hopeless and no mild case should be considered entirely safe. The author has seen cases that appeared most critical who subsequently recovered. On the other hand, he has observed comparatively mild cases that died suddenly, probably due to a cerebral embolus or ventricular fibrillation.

The ultimate prognosis, likewise, varies markedly Many cases survive the first attack and live many years with comparative comfort, and carry on a considerable amount of activity. Some of these may even, eventually, die from causes other than heart disease. Many others have recurring attacks and succumb to one of them Still others may die from congestive heart failure after a variable period of weeks, months or even years of invalidism

Treatment

In the treatment of coronary occlusion we must strive, first, to relieve the patient of his extreme suffering during the acute onslaught, and then carefully manage the effects of the infarction and any of the complications that may arise.

Control of the Acute Symptoms: The best and the only definite medication that will relieve the severe pain and other symptoms of the acute phase is morphine One-fourth of a grain should be given by hypodermic injection as soon after the onset as possible, and if sufficient relief is not obtained in twenty to thirty minutes another one-fourth grain is to be given. In some severe cases the author has employed as much as one grain within

two hours. In such cases, the suffering is very agonizing from the onset, and it is, therefore, more advisable to give the drug intravenously. When given by such route, the injection is to be made extremely slowly, and when the effect is produced the amount which is not used should be discarded

In occasional cases, the after-effects of morphine, such as nausea and vomiting are severe. In such cases, if the drug has to be repeated, we may try pantopan one-third grain or dilaudid one-twentieth grain by intramuscular injection, which in some instances appear to have no after-effects.

The wide use of papaverin and aminophyllin for relief of pain in the acute phases of coronary occlusion is of questionable value. In the author's experience he has never observed a case where the relief could definitely be attributed to those drugs We must realize that spontaneous cessation of pain and of other symptoms frequently occurs. If these drugs are used and the patient is relieved from pain in one to two hours we may be inclined to believe that such relief is due to the drug, whereas, actually it may be due to a spontaneous cessation of symptoms The author has used these drugs in many cases without any definite effect until morphine was given. In occasional cases where the pain is persistent for many hours, and is not fully relieved by morphine or its allied drugs, we may try aminophylline seven and one half grains by the intravenous route, in addition to the morphine A high concentration of oxygen given by the B L B mask, as described in Chapter XIII may be more valuable in such cases.

Management of the Early Phase· The first week or two is usually the most serious period from a view point of disturbing symptomatology and complications that may develop. If embolization, heart failure and other complications occur, this period may be prolonged for several weeks. During this phase, therefore, it is most essential that the patient have absolute bed rest General care should be the same as described in Chapter XIII for cases of complete cardiac decompensation.

The author's experience has been that any drug used during this period is valueless or may even be detrimental to the patient. The exceptions are morphine or its allied drugs if pain is recurring, or any of the barbiturates if extreme restlessness and insomnia occur. Demerol, in doses of 50 to 100 milligrams may often give symptomatic relief.

If profound shock persists and extreme drop in pressure continues and particularly if the patient is persistently or interruptedly pulseless, the outlook is usually hopeless. In such cases, we may try 50 cc. of 50 per cent glucose solution intravenously every three to four hours, or a continuous venoclysis of blood plasma or normal saline solution with 10 per cent glucose. The author has used this measure in an occasional case with temporary improvement, although the ultimate outcome was fatal, as it almost

always is, in such cases, regardless of what is used. However, the plasma or other fluid was not given in heroic amounts or rapidly enough for fear of overloading the seriously damaged heart. In this respect it is interesting to note the report of a case of extreme shock due to coronary occlusion by Schwartz.[38] This patient received 2200 cc. of plasma and blood within a period of forty minutes with rapid improvement of his condition and ultimate recovery.

In some cases of persistent shock, we may also try the use of caffeine sodium benzoate or coramine, although in the author's experience these drugs have no permanent value. It may, at times, temporarily improve the pulse. Caffeine should not be used in those cases that show marked restlessness and insomnia.

Cases where the heart rate is excessively rapid and a gallop rhythm is present, with evidence of a considerable degree of left heart failure, shown by moderate to marked acceleration of the respiratory rate and many congestive rales, should receive oxygen therapy. This, of course, should also be given to all cases where shock persists. The methods of administration of oxygen are described in Chapter XIII.

The food should be limited the first few days to small smounts of fruit juices sweetened with glucose, given at frequent intervals. When general improvement of the condition is noted, we may gradually add cereals, jello, junket and other light foods, as in congestive failure, described in Chapter XIII. The author considers vitamins B and C to be a valuable adjunct to therapy of this condition.

Constipation and abdominal distention should receive the care described in the chapter on congestive failure.

Anticoagulant Therapy: Recently, anticoagulant therapy came to the fore in the treatment of coronary occlusion. The object is to stop, if possible, the extension of thrombosis in the coronary vessels and to prevent the development of mural thrombi in the heart chambers as well as venous and arterial thrombosis in other parts of the body. Wright[39] reported 76 cases that were treated by this drug with favorable results. Several other favorable reports have appeared since. Greisman and Marcus[40] used this drug in 75 cases and found that the mortality rate was 9 per cent and the incidence of thromboembolic lesion 4 per cent. In a control group of 100 patients receiving conventional therapy, the mortality rate was 35 per cent and the incidence of thromboembolic lesions was 21 per cent. In view of the unusually high mortality rate in their control series we should allow for possible differences in the severity of the disease in the two series. Nevertheless the results of dicumarol therapy in their 75 cases is impressive.

From the latest series of 800 cases of coronary thrombosis treated with anticoagulants, as reported by a committee headed by Wright,[41] it appears

that dicumarol definitely reduces the mortality rate in this disease. The committee advocates its use in all cases of coronary thrombosis with myocardial infarction unless a definite contraindication exists.

The value of this therapeutic measure in this disease may, therefore, be considered to be well established, particularly in hospital cases where most of the admissions usually have the serious form of the disease. In the milder forms of the disease which are usually treated at home, and where private nursing care and attention are had, the conservative method of therapy may perhaps be safer This is true especially if the laboratory reports on the prothrombin time are not entirely reliable.

The author has followed a number of cases who received dicumarol therapy in private practice The general impression he formed, so far, is that the incidence of recovery in most cases which run a mild course is as great in patients who are treated conservatively as in those who get dicumarol therapy In more severe cases, however, the dicumarolized patients have a definitely better chance of recovery. The incidence of mild to moderately severe hemorrhage was greater in this series than in the hospital series reported so far This may partly be due to the unreliability of some laboratory reports on the prothrombin time.

Whether or not dicumarol influences the local extension of coronary thrombosis or increases the hemorrhagic infiltration in the infarcted area can not, as yet, be definitely determined It appears, from the experimental work by Beattie and co-workers[12] and by Blumgart and co-workers[13] that neither of these takes place

The dosage and manner of administration of the anticoagulants are discussed in Chapter XIX.

Management of the Arrhythmias: If the various arrhythmias develop they are to be treated the same as in other conditions described in previous chapters. There has been a tendency, recently, to use quinidine as a prophylactic measure to prevent the arrhythmias from developing in myocardial infarction. This was based on animal experimentation It seems to the author that the use of any drug with the anticipation that it may prevent something which occurs rather infrequently is unjustifiable. The drug, in itself, is not without harm. Furthermore, its effects are usually fast enough if used to stop an attack when it actually occurs

Management of Congestive Failure: Frank congestive failure occurring in myocardial infarction should be treated the same as in any other condition, as described in Chapter XIII Digitalis therapy, if necessary, is not contraindicated The belief that it may produce rupture of the heart or that it may predispose to embolization by the increase in the force of the cardiac contraction is not well founded. These accidents may happen

with equal frequency in cases that do not receive digitalis. Oxygen therapy is most beneficial

Duration of Bed Rest: Considerable controversy has been going on of late as to the length of time the patient is to be confined to bed Previously, a strict regimen of at least six weeks of bed rest was enforced on all patients regardless of the severity of the disease Lately there is a tendency for the pendulum to swing in the opposite direction Many clinicians advise only one to three weeks of bed rest. Experimentally, Thomas and Harrison[44] have shown that the mortality of rats with myocardial infarction was much greater when kept confined in small cages with restricted muscular activity than in those which returned to activity in three to seven days Also, on the basis of available evidence on men those authors believe that during the first two weeks the advantages of strict bed rest probably outweigh the disadvantages After that they feel that the reverse is probably true

I feel that the length of time a patient with coronary occlusion is to remain in bed should be based entirely on the extent of myocardial damage and the reaction of the individual patient to such damage A person who develops coronary occlusion which results in no myocardial damage should be allowed out of bed after three or four days of careful follow-up and the demonstration of the absence of such damage If a moderate amount of myocardial infarction is present, but the patient's reaction is good, being entirely symptom-free after the initial onslaught, and with little temperature reaction, lasting one to two days, the patient may be allowed out of bed three or at most four weeks after the attack If, on the other hand, the infarction is extensive and is associated with many complications, the patient is to be kept in bed at least four to six weeks, and in some cases much longer Each individual patient requires a careful determination of his cardiac injury from time to time, and his constitutional reaction to such injury, for proper advice No blanket rule can be given In general, it is wiser for various reasons, especially for its psychologic effect, to allow the patient out of bed as early as his cardiac condition warrants

Duration of Convalescence The length of time the patient is to have relative rest after recovery depends upon the extent of residual cardiac damage, the disturbances caused by such damage, the general constitutional state of the patient, his psychologic makeup and his financial status

If the residual cardiac damage is not marked and if the patient is practically symptom-free, he may return to some business activity three or four weeks after leaving his bed During this period he is to be allowed up and about, slowly, progressively increasing the amount of walking The effect of such activity on the heart is to be watched

If the residual cardiac damage is severe and the patient suffers from considerable dyspnea and precordial pain, the convalescence period must be prolonged *The length of time varies with the individual case* Some severe cases may require many weeks or months of convalescence before they can return to some gainful occupation. An occasional severe case may never be able to return to his accustomed work, especially if it is arduous and requires considerable concentration.

The psychologic makeup of the individual patient and his financial state are important factors in determining the length of time of convalescence If morose and depressed over the enforced rest, and if greatly embarrassed financially, resulting in worry and anxiety over the future, the patient is to be allowed to resume some gainful occupation as soon as possible In fact, some of these patients return to work against the advice of their physicians. Interestingly enough, many of them get along very well in spite of all rules to the contrary Whether or not early return to activity has an effect in ultimately shortening the patient's life by predisposing him to further coronary thrombosis or to a breakdown of the cardiac reserve is not definitely known The author's experience leads him to believe that such is the case, especially if the patient is not guarded as to the amount of activity by his physician. It is essential, however, not to instill any fear in the patient, and not to stress the danger of overstrain.

A general rule should be not to allow the individual case any more activity at any time than he can carry on without the slightest discomfort. Any effort which brings about precordial pain or dyspnea should be strictly prohibited It indicates that the particular effort has a straining effect on the heart and coronary supply In this respect the sensitive individual has a better chance of averting more serious future damage than one who has a low sensitivity.

REFERENCES

[1] Obrastzow, W P, and Straschesko, N D Zur Kenntnis der Thrombose der Koronararterien der Herzens Ztschr f Klin Med 71 116, 1910

[2] Herrick, J. B Clinical features of sudden obstruction of the coronary arteries. J A M A 59 201, 1912

[3] ——. Thrombosis of coronary arteries J A.M A 72 387, 1919

[4] Sigler, L. H The Electrocardiogram Its Interpretation and Clinical Application New York, *Grune & Stratton, 1944 Pages 244–275.*

[5] Vital Statistics—Special Reports, U. S. Department of Commerce Bureau of the Census. Vol. 25, No 6, June 26, 1946

[illegible] x, [illegible] J. 36 334, 1948.

Stryker, W. A.: Coronary occlusive disease in infants and children. Am J. Dis Child. 71:280, 1946.

9 Ravich, R. M, and Rosenblatt, P: Myocardial infarction in the newborn infant. Am J. Pediat 31·266, 1947.

10 Brown, H. R., and Pearson, R Seasonal variation in heart and coronary disease as related to various environmental factors Am Heart J. 35 763, 1948

11 Master, A. M, Dack, S, and Jaffe, H. L Factors and events associated with onset of coronary artery thrombosis J A M A 109 546, 1937.

12 Mintz, S S, and Katz, L. N Recent myocardial infarction Arch. Int Med 80 205, 1947

13 Fitzhugh, G, and Hamilton, B E Coronary occlusion and fatal angina pectoris Study of the immediate causes and their prevention J.A M A. 100 475, 1933.

14 Boas, E P Angina pectoris and cardiac infarction from trauma or unusual effort J A M A. 112.1887, 1939

15 Blumgart, H L The relation of effort to attacks of acute myocardial infarction J A M A 128 775, 1945

16 Paterson, J C Vascularization and hemorrhage of the intima of arteriosclerotic coronary arteries Arch Path 22 313, 1936

17 Leary, T Vascularization of arteriosclerotic lesions Am Heart J 16 549, 1938.

18 Wartman, W B Occlusion of the coronary arteries by hemorrhage into their walls Am. Heart J 15·459, 1938

19 Horn, H., and Finkelstein, L E · Arteriosclerosis of the coronary arteries and the mechanism of their occlusion. Am Heart J 19 655, 1940

20 Brown, M. R. A study of the pathogenesis of myocardial fibrosis "chronic fibrous myocarditis" Am. J M Sc 184 707, 1932.

21 Ravin, A, and Geever, E F Coronary arteriosclerosis, coronary anastomosis and myocardial infarction. Arch Int Med. 78 125, 1946

22 Schlesinger, M. J · An injection plus dissection study of coronary artery occlusions and [illegible]

23 [illegible]

24 [illegible] Acute myocardial infarction not due to coronary artery occlusion J A.M.A. 112.1675, 1939

25 Govier, W M The effect of experimental coronary artery ligation on the coenzyme 1 and cocarboxylase content of the myocardium of the dog Am Heart J 29 384, 1945

26 Race, G A, and Lisa, J R Combined acute vascular lesions of brain and heart Am J M Sc 210 732, 1945

27 Mendlowitz, M, Schaver, G, and Gross, L Hemodynamic studies in experimental coronary occlusion Am Heart J 13 664, 1937

28 Sigler, L H Case of coronary occlusion with complete heart block Ann Int Med 4 835, 1925, Treatment of the Stokes-Adams syndrome by hypertonic glucose given intravenously. Ann Int. Med 18 101, 1939.

29 Schwartz, S P: Auriculo-ventricular dissociation and the Adams-Stokes syndrome in acute coronary vessel closure Am Heart J 11 554, 1936

30 Master, A M, Dack, S, and Jaffe, H L Partial and complete heart block in acute coronary artery occlusion Am J M Sc 196 513, 1938

31 Wood, A M Perforation of the interventricular septum due to cardiac infarction. Brit Heart J 6 191, 1944.

32 Davis, D Spinal nerve root pain (radiculitis) simulating coronary occlusion A common syndrome Am Heart J 35·70, 1948

33 Blumer, G The importance of embolism as a complication of cardiac infarction Ann. Int Med 11.499, 1937

34 Eppinger, E C, and Kennedy, J. A The cause of death in coronary thrombosis, with special reference to pulmonary embolism. Am J. M Sc 195·104, 1938.

[35] Nay, R M , and Barnes, A R Incidence of embolic or thrombotic processes during the immediate convalescence from acute myocardial infarction Am Heart J 30 65, 1945
[36] Friedman, S , and White, P D Rupture of the heart in myocardial infarction, experience in a large general hospital Ann Int Med 21 778, 1944
[37] Conner, L A , and Holt, E The subsequent course and prognosis in coronary thrombosis An analysis of 287 cases Am Heart J 5 705, 1930
[38] Schwartz, W B The treatment of shock accompanying myocardial infarction Am Heart J 33 169, 1947
[39] Wright, I S Experiences with dicumarol in the treatment of coronary thrombosis with myocardial infarction Am Heart J 32 20, 1946
[40] Greisman, H , and Marcus, R M Acute myocardial infarction Detailed study of dicumarol therapy in seventy-five consecutive cases Am Heart J 36 600, 1948
[41] Wright, I S , Marple, C D , and Beck, D F Report of the committee for the evaluation of anticoagulants in the treatment of coronary thrombosis with myocardial infarction Am Heart J 36 801, 1948
[42] Beattie, E J , Cutler, E C , Fantaux, M , Kinney, T D , and Levine, H D The use of dicumarol in experimental coronary occlusion Am Heart J 35 94, 1948
[43] Blumgart, H L , Freedberg, A S , Zoll, P M , and Lewis, H D The effect of dicumarol on the heart in experimental acute coronary occlusion Am Heart J 36 13, 1948
[44] Thomas, W C , and Harrison, T R The effect of artificial restriction of activity on the recovery of rats from experimental myocardial injury Am J M Sc 208 436, 1944

CHAPTER XXI

Disease of the Aorta

THE AORTA is frequently the seat of degeneration and, at times, also of inflammation and of congenital abnormalities Due to these pathologic conditions, this artery may be subject to stretching, aneurysmal dilatation and rupture, like any other artery of the body.

In the majority of cases, aortic disease is asymptomatic Symptoms and signs develop when pathologic changes affect the aortic valve or the coronary ostii, or when a large compressing aneurysm develops. Acute manifestations are those caused by rupture or dissection of this vessel.

Aortic Degeneration

Atheromatosis is the most common form of aortic degeneration. It is so prevalent, especially after 45 years of age, that very few autopsy cases after that age are free from it. It is also frequently observed in individuals below 45 years and, occasionally, even in youth Accompanying the atheromatosis, there is progressive hardening of the aorta, like other vessels, with advancing age The pathologic changes have been described in Chapter XIX.

As a result of such changes, the aorta becomes tortuous and dilated The dilatation is usually diffuse, although it may be more pronounced in the ascending portion The condition, as a rule, is asymptomatic Precordial pain may be present but it is questionable whether it is due to the aortic disease or to associated coronary sclerosis The widening of the aorta may be recognized by an increased area of dullness to the right of the sternum in the second and third interspaces, by suprasternal pulsation and by roentgenologic examination, as described in Chapter X

Besides the widening and tortuosity, marked atheromatosis will produce a denser x-ray shadow than normally. It must be remembered, however, that a roentgenologic examination of the aorta may often yield greater dilatation than is actually present and shown at autopsy This dilatation is due to its dynamic distention during life caused by intra-aortic pressure.

A systolic murmur is often heard over the aortic area in cases where the ascending portion of the aorta is more or less dilated Where the dilatation is very marked, some degree of functional aortic insufficiency may occur in rare cases Definite aortic insufficiency is caused by structural changes in the valve

A rare form of aortic degeneration is that of "idiopathic cystic degeneration of the media," described by Erdheim[1] This may lead to dissecting aneurysm of the aorta as described later in the chapter.

Syphilitic Aortitis

Inflammation of the aorta may occur in any acute or subacute infectious disease such as typhoid, pneumonia, rheumatic fever or from extension of any thoracic infections or from septic embolization in subacute bacterial endocarditis Such aortic involvement is comparatively rare and our attention must be directed to the original disease of which inflammation of the aorta is only a complication

The most important inflammatory process involving the aorta is that caused by *syphilis* This is due to the relative frequency of syphilis and its specific predilection for the aorta Although the infection may involve also the heart, producing either localized gummatous or diffuse myocardial changes, such involvement is rare Warthin[2] considered that syphilitic myocarditis and myocardial fibrosis occurred more frequently than we thought and he believed that he demonstrated the presence of Spirochaeta pallida by special staining methods This has been refuted, however, by Saphir[3] and other investigators.

Etiology

The underlying cause of syphilitic aortitis is of course the Spirochaeta pallida This organism appears to have a predilection for the aorta There is a latent period of ten to twenty years between the primary lesion and the clinical manifestations of aortic disease Although slow pathologic changes undoubtedly take place during this period, they are not detectable clinically

The entrance of the organism is presumably through the vasa-vasorum of the aorta, or through the mediastinal lymphatics The lodging places of the organism are in the adventitia and media.

Because of the prolonged latent period between the primary lesion and the manifestations of aortic disease, the usual ages at which luetic aortic involvement occurs most frequently are between 30 and 50 years, the majority of cases being in the fourth decade In this country, it is more common in the South because of the greater Negro population. It occurs more among males than females Ignorance and lack of proper medical care of the primary and secondary stages of syphilis are the most important predisposing causes of the later stages of the disease

The frequency of cardiovascular involvement in syphilis has been found on autopsy to vary between 70 and 80 per cent by Langer.[4] Clinically, however, Cochems and Kemp[5] found that of 1,000 syphilitic individuals, only 12 7 per cent showed evidence of cardiovascular syphilis. Evidently a great many cases are overlooked The incidence of luetic aortitis among the general population varies between 2 and 6 per cent in different reports. The incidence, however, appears to have definitely diminished within the past decade.

Pathology

In the well developed lesion, the gross appearance of the inner part of the aorta is that of elevated, gray translucent patches running lengthwise from about the sinus of valsalva all through the thoracic and occasionally even the abdominal aorta. They may be discrete or they may coalesce, forming larger patches. The condition gives the aorta a "tree bark" appearance

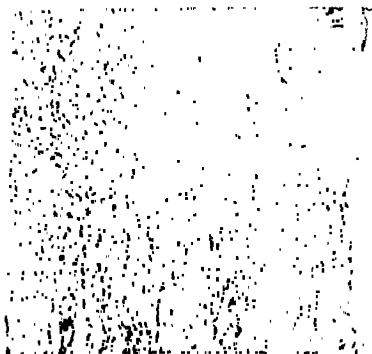


FIG 99—SYPHILITIC AORTITIS Collections of round cells and fibroblasts around the vasa-vasorum in the adventitia and media with necrotic changes in the media × 30

The microscopic findings consist, in the early stages, according to Saphir and co-workers,[6] of obliterative endarteritis of the vasa-vasorum Necrosis of the media results from nutritional disturbances The very early changes consist of collections of small round cells, fibroblasts and many plasma cells in the adventitia and around the vasa-vasorum in the media, as shown in Figure 99 These small vessels are narrowed and in some places entirely obliterated. Later, much of the elastic and connective tissue of the aorta undergo hyaline degenerative changes, and strands of broken elastic tissues are widely separated from each other The space between is replaced by connective tissue representing an attempt at reparative proc-

esses The intimal cells increase in number and necrotic changes occur in the media.

As a result of these changes, the vessel wall is weakened and some areas may develop various small sized aneurysms. If the process is widespread, thinning of the entire thoracic aorta or large portions of it takes place, resulting in large diffuse or sacculated aneurysms. If the process affects the coronary orifices, narrowing takes place, interfering with the coronary blood supply Narrowing or partial obstruction of the other branches arising from the aorta may also take place. If the process extends toward the aortic valve, commissural separation and scarification of the cusps will occur, leading to their shortening and retraction and thus to aortic insufficiency

Clinical Manifestations

Because of the stealthy and very slowly progressing character of the disease, syphilitic aortitis may go on for many years without recognition Usually, when the process reaches the clinically recognizable stage, there is irreparable damage We have neither definite physical signs nor characteristic symptoms by which the disease may be diagnosed in the early stages It should, however, be suspected if, in the pre-arteriosclerotic age, a patient with a history of a primary lesion or a positive serology develops precordial pain and a loud tambour-like aortic second sound In addition, if a roentgenologic examination reveals some widening or irregularly shaped aorta with increased pulsation, the presence of the disease may be more certain. *This is true especially in the absence of marked and persistent hypertension*

Luetic aortic involvement may be more definitely diagnosed either where aortic insufficiency is present or when signs and symptoms point to aortic aneurysm or when signs and symptoms of coronary insufficiency develop in the pre-arteriosclerotic age with a history of lues. Although these three conditions are often considered complications of luetic aortitis, they are really merely advanced stages of the disease with particular localization in given areas of the aorta

Luetic Aortic Insufficiency This is considered to be of luetic origin if there is no history of rheumatic fever or hypertension and if it develops in the pre-arteriosclerotic age If the patient presents aortic insufficiency for the first time after 50 years of age, it still may be considered to be of luetic origin if there is a history of lues and if no marked hypertension and arteriosclerosis are present It must be borne in mind that often more than one etiologic factor may be responsible for the lesion If aortic insufficiency is coexistent with mitral pathology, there is a likelihood that rheumatism is the underlying cause It must be remembered, however, that in late aortic insufficiency, a systolic murmur may be heard at the apex and in some cases,

also a presystolic—the so-called Austin Flint murmur. Care must therefore be taken in arriving at a definite diagnosis of coexistent mitral pathology The subject is more fully discussed in Chapters IX and XXIV

Luetic Aortic Aneurysms These are usually single but they may be multiple Their sizes vary from one to upward of twenty centimeters in diameter They are most frequently located in the ascending aorta, but they may occur in the transverse arch, in the descending or in the abdominal portions

In many cases, an aortic aneurysm may yield no signs and symptoms and may be discovered accidentally, roentgenologically or on postmortem examination When, however, it is large or it exerts pressure on important structures, there are certain symptoms and signs by which it may be recognized

An aneurysm of the ascending aorta is accompanied in about 10 per cent of cases by aortic insufficiency If the aneurysm is small and is *located in the sinus of Valsalva*, it may go unrecognized If, however, it compresses the pulmonary artery, it may be followed by right ventricular enlargement and ultimate failure The condition may be suspected where right ventricular enlargement and signs of right heart failure occur in the absence of pulmonary pathology or other conditions predisposing to such failure and in the presence of a history of lues and aortic insufficiency. Brill and Jones[7] find that a continuous machinery-like murmur heard over the pulmonic area similar to that of patent ductus arteriosus may be an additional sign Rupture of these aneurysms may take place into the pericardial cavity, the right ventricle, the pulmonary artery or into the right auricle

According to Hermann and Schofield[8] rupture of an aortic root aneurysm in these areas presents a characteristic syndrome which is practically the same in all locations The premonitory signs are boring, burning or aching pain in the region of the aortic root, pulmonary artery dilatation, and accentuation of the pulmonic second sound The rupture is characterized by abrupt collapse, shock, extreme exhaustion, weakness and dyspnea A long, harsh continuous murmur and thrill develop at the mid-sternal region most intense when sitting up, leaning forward or holding the breath If the fistula is between the aorta and right auricle, there is a smothering, tightness and fullness in the chest A characteristic rough to-and-fro machinery-like murmur develops in the midsternal region, transmitted along the right border Right heart failure ensues in all cases

An aortic aneurysm arising higher than the sinus of Valsalva, if unassociated with aortic insufficiency, may be silent until it becomes very large An interesting example is shown in Figure 100, from a male 42 years old He presented no symptoms for several years, until the aneurysm began to bore its way through the anterior chest wall.

An aneurysm originating mainly in the *arch* is usually not strictly localized to the transverse portion but extends to the ascending or descending portion It may, at times, be localized mainly at its junctions with the ascending or descending parts. Like aneurysms in other parts of the aorta, these may also be silent in some cases In many cases, however, these aneurysms yield the following symptoms and signs.



Fig 100.—Massive Syphilitic Aneurysm of the Ascending Aorta with Some Calcification of its Wall Male 42 years old.

Symptoms: The most common symptoms are pain, dyspnea, cough, hoarseness and dysphagia These symptoms may appear singly or in combination, depending upon the organ or structure which the aneurysm compresses.

The most frequent complaint is *pain* which is usually felt in the anterior chest wall, in the back or in the neck and rarely in the arms. Unlike the pain of angina pectoris, the pain here is not increased by excitement or exertion. It is, however, frequently aggravated when the patient changes his posture. It is often described as severe, persistent and boring. It



Fig. 101.—Antero-posterior view, barium esophagram. Esophagus is compressed and displaced to the right by an aneurysm of the transverse arch. Heart slightly enlarged.

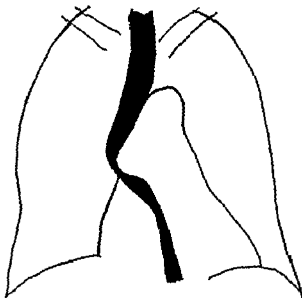


Fig. 102.—Copy of Fig. 101, Showing the Features more Clearly. The esophagus is shown in black.

occurs when the aneurysm compresses and erodes any part of the bony structure of the chest.

Dyspnea occurs only when the aneurysm is very large and compresses the trachea or bronchi or displaces a large part of the lung.



FIG 103 —LEFT OBLIQUE VIEW, SAME PATIENT AS IN FIG 101 Compression and displacement of esophagus anteriorward, by the aneurysm.

Cough, if present, is nonproductive and in the early phases it is of the hacking or "brassy" type *Later, if there is considerable compression of* the trachea, or of a bronchus, the cough may become productive and may, at times, be blood tinged.

Hoarseness occurs in those cases where the aortic arch is markedly

years old, presented some hoarseness, difficulty in swallowing, cough, and some dyspnea The symptoms dated back about two years, but became progressively more severe. About one month before the examination the hoarseness was very marked and the swallowing became rather difficult. There was some paralysis of the vocal cords, due to pressure on the recurrent laryngeal nerve He showed generalized arteriosclerosis, moderate hypertension, and evidence of luetic involvement of the central nervous system His blood Wassermann was markedly positive, as was the spinal

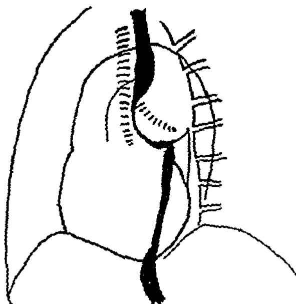


FIG 104—COPY OF FIG 103, SHOWING THE FEATURES MORE CLEARLY The esophagus is shown in black

fluid An ordinary roentgenologic examination of the chest in the antero-posterior view showed only slight widening of the aorta and some cardiac enlargement Barium esophagrams obtained in the antero-posterior and lateral views, shown in Figures 101, 102, 103, and 104, reveal a massive aneurysm at the junction of the transverse and descending portions of the arch in its lower part, compressing the esophagus, anteriorward and to the right. He died suddenly, three months after the x-rays were obtained, from a rupture of the aneurysm into the esophagus resulting in a copious and fatal hemorrhage through the mouth.

Physical findings An aortic aneurysm, if large enough and located mainly in the transverse arch, may produce certain signs, depending upon its location and the direction of its protrusion.

The signs may consist of inequality of the pupils, increase in the area of aortic dullness, expansile pulsation, engorgement of the veins, tracheal deviation and tug and inequality of the radial pulses and blood pressure readings in the two arms

Inequality of pupils is due to irritation of the sympathetic nerves. In many cases, it may occur in luetic involvement of the central nervous system without an aortic aneurysm.

Increase in the area of dullness to the right of the sternum, in the second to the third interspace, may occur in an aneurysm located in the junction of the ascending portion of the aorta and the transverse arch Dullness in the left lower interscapular region may occur in a descending aneurysm.

Expansile pulsations may be seen and felt in the corresponding areas if the aneurysm is large and in contact with the chest wall If the bony structures of the chest in these areas are destroyed, the pulsating mass may protrude above the surface of the chest and the skin over it becomes tightly stretched

Engorgement of the veins in the neck, upper chest and arms may occur if an ascending aneurysm compresses the superior vena cava

Tracheal deviation from the midline is often seen in aneurysms at the junction of the transverse and descending portions of the arch In some of these cases, there may also be a tracheal tug due to pulsation of the aneurysm which pushes the left bronchus down with each expansion

Inequality in the pulses and blood pressure readings in the two arms are to be considered merely aids in the diagnosis, if other evidence points to the presence of an aneurysm, for these findings are often observed in other conditions, as described in Chapter X.

Osteal Coronary Narrowing and Occlusion: Luetic involvement in the regions of the coronary openings in the aorta will produce the anginal syndrome or congestive failure as in coronary disease, described in Chapters XIII and XIV. Complete occlusion of the orifices seldom occurs In some cases, myocardial infarction may develop even if occlusion is not complete.

It is often impossible to tell if the symptoms of coronary insufficiency are due to coronary disease or osteal coronary involvement. In the presence of demonstrable luetic aortic aneurysm or aortic insufficiency, especially in the pre-arteriosclerotic age, coronary insufficiency may be considered to be due to osteal coronary involvement.

Treatment

Treatment of syphilitic cardiovascular disease should be preventive. Early syphilitic manifestations must receive thorough therapy in order to prevent aortic involvement. Once such involvement has progressed to the [illegible] directed to the syphilitic condition is [illegible] harmful in some cases.

[illegible] xt to describe the therapy of early

syphilis. We will confine our attention only to the late stage when recognizable cardiovascular disease is evident. At this stage the therapy of lues should be very conservative, and attention must be concentrated on the prevention of cardiac failure, where possible, and on the treatment of such failure if present. Only when no cardiac failure is present, or when such failure is under control may we attempt to treat the syphilitic condition itself Even then, we must be extremely careful not to overtreat the condition.

There are three serious conditions that may develop as a result of active arsenical therapy of syphilis at this stage They are the Jarisch-Herxheimer phenomenon, the nitroid reaction, and the so-called therapeutic paradox

The Jarisch-Herxheimer phenomenon consists of malaise, fever and a flare-up of syphilitic lesions The coronary ostii may suddenly be closed by the reactive edema of the aorta, resulting in sudden death If an aneurysm is present it may suddenly dilate and even rupture

The nitroid reaction exhibits itself in the form of dyspnea, cough, flushing of the face, and occasionally loss of consciousness It may occur during the injection or soon after

The therapeutic paradox consists of a period of temporary improvement followed by protracted congestive failure, which can not be controlled.

To avoid these accidents it is essential that the arsenicals be withheld or used extremely cautiously in this stage of syphilis If congestive failure is present, therapy should be employed as described in Chapter XIII In addition, potassium iodide may be administered in doses of 5 to 10 grains, and gradually increased to 20 or 60 grains three times a day, if well tolerated

In the absence of decompensation, or if compensation is restored, small doses of insoluble bismuth—such as bismuth subsalicylate in oil may be given intramuscularly every five days for several weeks, starting with 02 gram, and increasing gradually to 0 2 gram Its effect must be carefully watched A rest period of several weeks should then be given during which iodides alone are to be used This is followed by another course of bismuth and iodides for several weeks. The treatment is thus continued for one or two years If no improvement in symptoms is obtained, or untoward effects develop, the treatment should be discontinued sooner

The management of this stage of syphilis recommended by the Veterans Administration[9] under Schedule B, consists of penicillin only, not the arsenicals or bismuth A total of 6,000,000 units is administered in 120 individual doses of 50,000 units each at three hour intervals day and night over a period of fifteen days. To avoid the various reactions discussed above, the patient is first given 5,000 units for twenty-four doses before the 50,000 unit doses are started for 120 more injections. If so desired, bismuth subsalicylate in oil may be given once a week for four weeks, and then 50,000 units of penicillin may be employed per dose from the onset.

In cases of large aortic aneurysms which bore their way through the chest wall, and produce severe pain with danger of rupture, Poppe[10] recommends cellophane treatment. The aneurysm is exposed and is covered by Polythene cellophane. This material produces dense fibrous tissue reaction *which curbs the aneurysmal pulsation, expansion and its tendency to rupture* He has treated six cases successfully by this method with relief of pain and without disturbing effects from the cellophane, so far, over a period of a few months to two years

Incomplete Rupture of the Aorta

Peery[11] calls attention to rupture of the intima of the aorta which has been unrecognized clinically and on postmortem examination in the past. He reviewed the literature on the subject and reported eleven cases of his own

An intimal tear may result in a dissecting aneurysm, or it may heal. The tear usually affects the ascending portion near the commissures and is mostly in a transverse or oblique direction, although in rare cases, it may be longitudinal. The reason for the frequent localization of a tear in this location is probably the relative immobilization of this portion of the aorta. The tear may measure 0 5 to 2 centimeters in its transverse diameter and its edges are sharp The lips of the tear may extend 2 to 6 centimeters apart. Multiple tears may occur in some cases

The main underlying cause appears to be marked hypertension. The precipitating factors in some cases may be severe strain, exertion and, at times, trauma The rocking force of the aortic leaflets may help bring about such rupture for, as said before, it occurs most frequently near the commissures

There are no characteristic symptoms by which the condition may be recognized clinically In some of the cases, the patient experiences a choking sensation, dyspnea and a suffocating feeling, as well as stabbing or tearing upper sternal pain The condition should be suspected in cases with hypertension who suddenly develop these symptoms and particularly where murmurs develop at the aortic area soon after the onset of such symptoms. These murmurs are probably produced by distortion of the aortic leaflets caused by the tear.

Dissecting Aneurysm of the Aorta

This consists of a hemorrhage dissecting its way through the media of the aorta. In many, but not all cases, the intima is broken through.

According to Sailer,[12] the condition was first described by Nicholes as long ago as 1761, and although numerous autopsy cases have been reported since that time, clinically, the condition has rarely been diagnosed until recent years In a series of 300 cases collected from the literature and 17 cases of his own, Shennan [13] found only 7 cases where the diagnosis was made ante-

mortem Glandy and co-workers[14] reported 19 cases, 2 of which were diagnosed antemortem With more careful correlation of autopsy and clinical findings in recent years, however, more frequent clinical diagnoses are reported Thus, Warren and McQuown[15] recently reported a correct antemortem diagnosis in 3 out of 5 cases that came to autopsy. In another recent report of 45 cases by Baer and Goldburgh[16] 11 were diagnosed clinically.

Incidence The incidence of dissecting aneurysm of the aorta is not definitely known In the different reports from the literature cited by Bauersfeld[17] it varied between 0 14 and 0 7 per cent of all autopsy cases. He also found that of all cases of sudden nontraumatic deaths in San Francisco, 1 1 per cent were due to dissecting aneurysm of the aorta Warren and McQuown[15] found an incidence of 1 out of each 454 autopsies performed in the Charity Hospital of Louisiana This corresponds approximately with the incidence reported by Blandy and co-workers

The condition occurs much more frequently after 40 years of age but there are many cases on record of younger individuals In a review of 580 cases from the literature, Schnitker and Bayer[18] found 141 cases or about 24 per cent in persons under 40 years of age In Shennan's series, however, more than 80 per cent were over 50 years of age Cases younger than 30 years are extremely rare There is a much greater incidence in males than in females.

Underlying Causes The underlying causes of dissecting aneurysm of the aorta are not definitely known. Hypertension may play a part in the old age groups, although in itself it probably is no factor, inasmuch as a great many of the reported cases had normal blood pressure, while comparatively few individuals with extremely high blood pressure developed it Furthermore, Schattenberg and Ziskind[19] quote Oppenheim who found that it takes two to three thousand millimeters of pressure to rupture the aorta in a fresh cadaver Strain and trauma apparently play a part in some cases, although it often occurs at rest Syphilis and atheromatosis of the aorta, likewise, apparently play no part Although these conditions, especially the latter, have been found in many of the cases, the dissection in those cases usually does not originate from an atheromatous area In pregnant women and during the postpartum period where the condition has occurred apparently spontaneously, Schnitker and Bayer postulate the theory that altered blood lipoids occurring during this period lead to changes in the media which predispose to the condition

The Underlying Pathology· The structural pathology which leads to a dissecting aneurysm is most likely some degeneration in the medial layer In two cases presented by Schattenberg and Ziskind idiopathic cystic medionecrosis of the aorta, described by Erdheim, was present and this may be

the underlying cause in many other cases Additional pathologic findings are either congenital hypoplasia of the aorta or coarctation, both of which have been frequently observed in many cases of the younger age groups These cases probably have some congenital thinning or weakness of the media

The dissection is believed to begin as a hematoma in the degenerative media which, if large enough, causes rupture of the overlying intima Dissection then begins as a result of the intra-aortic pressure sending a column of blood into the torn part

Clinical Manifestations: The clinical manifestations of a dissecting aneurysm vary with the extent of the dissection and with the rapidity of its onset The patient is usually seized with sudden excruciating, constricting, stabbing or cramp like pain in the retrosternum or precordium with very wide radiation extending as far as the lower spine and even to the legs The most frequent radiation is to the interscapular region and to the neck The pain is similar in character to that of coronary occlusion but is usually much more severe, has a more widespread radiation and does not have the tendency to radiate to the arms which it frequently does in occlusion

With the pain, there is often a marked choking sensation or suffocation and syncope If the dissection does not progress to any great extent, these symptoms may abate in several hours If, however, the condition is progressive, occlusion of the various vessels springing from the aorta may slowly take place resulting in interference with the blood supply to the corresponding organs Thus, coronary osteal occlusion may be followed by myocardial infarction and its characteristic signs and symptoms Interference with the blood flow through the carotid arteries may result in cerebral disturbances such as vertigo and syncope. Occlusion of the orifices of the renal arteries may result in lumbar pain, hematuria, renal insufficiency and uremia. If it extends to the bifurcation of the aorta with obstruction to the common iliac arteries, the effects on the lower extremities may be the same as from embolization in those vessels. Thus, the symptomatology is protean in nature, corresponding to the interruption of the blood supply which the aorta, as the main trunk, and its various branches carry to different parts of the body

The physical findings will, of course, correspond to the organs involved Inasmuch as the process originates in the first part of the ascending aorta near the commissures, in the majority of cases, widening of the area of dullness in the second and third right interspaces and the developement at first of a systolic murmur and later also of a diastolic murmur in the aortic area, are the outstanding findings of the condition. The diastolic murmur is caused by distortion and some displacement of the aortic leaflets and unlike the diastolic murmur due to aortic valvular disease which is soft, the

murmur here may be rough Elevation in temperature to 101 degrees F. or somewhat higher may occur and leukocytosis may develop.

Diagnosis of Dissecting Aneurysm: In the early phases, a dissecting aneurysm of the aorta must be differentiated from coronary occlusion, pulmonary and peripheral embolization, an acute surgical abdomen and various other conditions discussed in the chapter on acute coronary occlusion. If the condition occurred after strain or trauma it must also be differentiated from ruptured aortic cusps

In dissecting aneurysm, as pointed out before, the pain is usually of greater severity than in coronary occlusion. Its radiation to the spine occurs more frequently and to the arms less frequently than in coronary occlusion. The blood pressure in most cases does not fall Syncope is frequent. The development of murmurs frequently occurs and often a broadening of the base to the right of the sternum is observed A pericardial friction rub does not appear The electrocardiogram remains normal and if some abnormalities are present, they are not characteristic of coronary occlusion.

In ruptured aortic cusps, the diastolic murmur is pronounced from the very start and has usually a loud rasping or musical quality. Aortic dilatation and cardiac enlargement develop later.

The diagnosis of embolization has been described in Chapters XVIII and XIX

In the later phases, if the patient survives, a dissecting aneurysm must be differentiated from a syphilitic aortic aneurysm and aortic dilatation due to sclerosis and hypertension In both of these conditions, there is no history of an acute episode which was followed by the aortic changes. A negative blood Wassermann may help, but does not always rule out syphilis

Prognosis The ultimate outcome of a dissecting aneurysm of the aorta varies In about 80 to 90 per cent of cases, rupture of the aortic wall occurs through the adventitia with hemorrhage into the pericardium, pleura, mediastinum or abdominal cavity, resulting in sudden death. In most of these cases, rupture occurs into the pericardial cavity. The remaining 10 to 20 per cent of cases recover from the first attack, and in one half of these further dissection recurs, ending ultimately in death caused by rupture Some cases, apparently recover completely by organization and even by endothelialization of the inner part of the aneurysm. Some of the cases may ultimately die from other causes or from left heart failure

The following example of a dissecting aneurysm of the aorta has certain points of interest A healthy looking male, 26 years old who never had any complaints, was on his vacation and partook of a heavy breakfast followed by two strenuous games of handball and then baseball While playing, he developed severe, agonizing pain in the upper sternal region and in the lower thoracic spine, with extreme difficulty in breathing, and collapse He was

taken to a hospital where he recovered from the symptoms in about two and a half hours and was comfortable thereafter. He stayed in the hospital about three weeks. The diagnosis of coronary occlusion was made The author saw him for the first time about five weeks after the attack. At that time, he had no complaints. The essential findings were moderate bulging of the ascending aorta which stood out distinctly from, but merged with the right auricular border The bulging was somewhat irregular. The left ventricle was slightly enlarged These features are shown in Figure 105.



FIG 105—DISSECTING ANEURYSM OF THE AORTA The aorta is markedly widened and there is bulging in the ascending portion, shown by arrow, which extends beyond the right auricular border and lower than normally See text

The aortic second sound was markedly accentuated and there was a short systolic murmur heard at the aortic area transmitted to the right clavicle. No diastolic murmur was heard His blood pressure was 160 to 170 systolic and 100 to 110 diastolic The electrocardiogram was normal and showed a tendency to left axis deviation Several of his electrocardiograms obtained from the hospital showed the same findings with no changes in the configuration of the complexes from time to time. The author's diagnosis was dissecting aneurysm of the ascending aorta Traumatic rupture of the aortic valve was ruled out by the absence of a diastolic murmur. Coro-

nary occlusion was ruled out by the aortic findings and by the absence of electrocardiographic changes

He came for re-examination about 8 months later with complaints of recurring pain in the right upper chest and throat appearing spontaneously in paroxysms, lasting twenty to thirty minutes, several times a day for four days. He was comparatively symptom-free up to that time. Examination now showed some increase in the bulge of the ascending aorta and a short loud diastolic murmur was heard at the aortic area in addition to the systolic murmur All other findings were about the same as before. The impression was that the dissection had extended and involved the region close to the aortic leaflets with distortion of the aortic valve. About 17 months later, he was found dead in his car

The essential autopsy findings consisted of a large dissecting aneurysm of the aorta with a fresh rupture into the pericardial cavity resulting in cardiac tamponade. There was a congenital hypoplasia of the aorta and a fusiform aneurysmal dilatation of the ascending portion measuring 7 centimeters in its greatest diameter, made up of media The aorta was double channelled, one lumen being continuous with the aortic valve and the other with the aortic aneurysmal pouch The opening of this pouch consisted of a tear in the intima about 3 5 centimeters above the sinus of Valsalva and measured about 4 by 1 5 centimeters The aortic valve was 8 centimeters in circumference, and its cusps were slightly thickened and its margins rolled.

This case is presented because of the unusually early age at which the condition developed and the comparative absence of symptoms for long periods between episodes of dissection It also illustrates the importance of bearing this disease in mind at any age in the diagnosis of an acute cardiovascular insult

Treatment Treatment of a dissecting aneurysm of the aorta is about the same as that of coronary occlusion Morphine should be given in sufficient amounts to relieve the severe early symptoms Prolonged absolute bed rest is to be enforced If recovery takes place, the patient is to lead a very quiet life He must be warned that any severe effort or strain may result in serious consequences

Complete Rupture of the Aorta

Complete rupture of the aorta without previous dissection occurs comparatively rarely, although a number of cases are reported in the literature The subject has recently been reviewed by Tayler and Morehead [20]

In most cases, there are extensive pre-existing aortic pathology, such as luetic aneurysm, marked atheromatosis and necrotizing changes of the wall, infiltration of the wall by metastatic malignancy or by extension of adjacent

tubercular or septic processes, marked congenital defects of the wall such as hypoplasia and coarctation, unusual thinning of the wall and the presence of mycotic aneurysms In all these cases, rupture may occur as a result of comparatively minor external trauma or sudden strain In rare cases, rupture of an apparently normal aorta may occur as a result of severe trauma, especially during the height of systolic filling

In most cases, death occurs almost instantaneously after a few gasps and convulsive movements, preceded momentarily by terrific pain. In some cases, the patient lives long enough to allow some clinical observation to be made which may suggest the diagnosis

In some cases, the perforation may be extremely small, even the size of a pinpoint at the bottom of an aneurysm, or in an ulcerated area, resulting in slow bleeding In such cases, spontaneous healing may occasionally take place In the majority of such cases, however, there are recurring ruptures with an ultimate fatal outcome

REFERENCES

[1] Erdheim, J Medionecrosis Aortae Idiopathica. Virchow Arch f Path. Anat 273 454, 1929

[2] Warthin, A S The new pathology of syphilis Am J Syph 2.425, 1918.

[3] Saphir, O Syphilitic myocarditis Arch Path 13 266, 1932

[4] Langer, E Die Haufigkeit der luetischen organveranderungen, ins besondere der aortitis luetica. Munchen Med Wchnschr 73 1782, 1926

[5] Cochems, K. D, and Kemp, J E Studies in cardiovascular syphilis II. The incidence of syphilitic aortitis A study of 1,000 syphilitic individuals Am J Syph, Gonor & Ven. Dis 21 282, 1937

[6] Saphir, O, and Scott, R W. Involvement of aortic valve in syphilitic aortitis Am J Path 3 527, 1927.

[7] Brill, I C., and Jones, R S The syndrome of compression of the pulmonary artery by a syphilitic aortic aneurysm with or without arterio-arterial communication Ann Int Med 24 111, 1946.

[8] Hermann, G R, and Schofield, N D The syndrome of rupture of aortic root or sinus of Valsalva aneurysm into the right atrium Am Heart J 34 87, 1947

[9] Veterans Administration The management of syphilis J A M A 134 1535, 1947

[10] Poppe, J K Cellophane treatment of syphilitic aneurysms with report of results in six cases Am Heart J 36 252, 1948

[11] Peery, T M Incomplete rupture of the aorta, A heretofore unrecognized stage of dissecting aneurysm and a cause of cardiac pain and cardiac murmurs Arch Int Med 70 689, 1942

[illegible] No 193, [illegible] orta Am Heart J 13 129, 1937

[15] Warren, A S, and McQuown, A L Dissecting aneurysms Presentation of ten case reports and a correlation of clinical and pathologic findings Am J. M Sc. 215 209, 1948

[16] Baer, S, and Goldburgh, H. L. The varied clinical syndromes produced by dissecting aneurysm. Am. Heart J 35.198, 1948

[17] Bauersfeld, S. R · Dissecting aneurysm of the aorta A presentation of fifteen cases and a review of the recent literature Ann Int Med 26 873, 1947
[18] Schnitker, M A, and Bayer, C A Dissecting aneurysm of the aorta in young individuals, particularly in association with pregnancy, with report of a case Ann. Int. Med. 20:486, 1944
[19] Schattenberg, H J, and Ziskind, J · Dissecting aneurysms of aorta J Lab & Clin Med 24:264, 1938
[20] Taylor, F. R, and Morehead, R P Spontaneous complete rupture of the aorta without dissecting aneurysm with report of a case showing a new physical sign Ann Int Med 21 81, 1944

CHAPTER XXII

Rheumatic Fever and Rheumatic Heart Disease

Because of its frequent involvement of the heart, rheumatic fever is one of the most devastating diseases in early life It is responsible for more crippling disability and death from heart disease, up to middle age, than any other etiologic factor

Incidence

According to Vital Statistics Special Reports,[1] there were 27,010 deaths from rheumatic fever and chronic rheumatic heart disease in the United States in the year 1944. This does not include deaths from chronic valvular and myocardial disease of unspecfied etiology numbering 41,227 and 213,930 respectively, many of which were undoubtedly of rheumatic origin An approximate estimate of deaths due to rheumatic fever and rheumatic carditis would, perhaps, run close to 50,000 for that year. Wyckoff and Lingg[2] estimated in 1926 that 25 per cent of all deaths from heart disease were of rheumatic origin Inasmuch as the total death rate from heart disease in that year was 206,188, the number of deaths due to rheumatic heart disease would thus be 51,547

The morbidity incidence of rheumatic fever is not known, because it is not a reportable disease. Some fragmentary studies, however, give us an idea of its extent For instance, among 33,297 school children examined in Philadelphia, Cahan[3] found an incidence of over 1 per cent of rheumatic valvular disease Various reports by other authors show an incidence of of 0 5 to 3 5 per cent in different parts of the country. According to Swift and McEwen,[4] of all admissions to New York University Division of Bellevue Hospital in New York City in 1935, 4.3 per cent were those of rheumatic fever.

Due to improved standards of living, better hygienic care and proper food, the incidence of rheumatic fever and rheumatic carditis has been on a gradual, but progressive decline in the past two decades This was demonstrated in a comparative study made by the Metropolitan Life Insurance Company, on the prevalence of heart disease among draftees in the first and second world wars, as shown in Figure 106

Etiology

The Predisposing Causes: These may be classed under hereditary and environmental, age, climate and season.

The relative importance of *heredity* and *environment* as predisposing causes have not as yet been definitely determined From a statistical study, Wilson[5] believes that the susceptibility to the disease is transmitted as a single autosomal recessive gene. On the other hand, from a recent analysis of 3594 rheumatic fever patients, and 1397 controls in the armed services of World War II, Griffith and co-workers[6] conclude that there does not appear to be a strong inherited susceptibility to the disease They believe that the occurrence of multiple cases in families is to be explained on the basis of contagion and common environment.

The *environmental* factors as predisposing causes consist of poor hygienic surroundings, including improper feeding, overwork, lack of cleanliness and

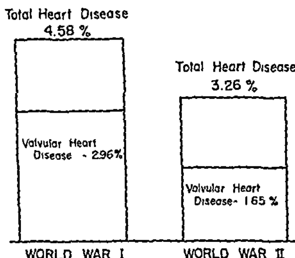


FIG 106—A COMPARATIVE INCIDENCE OF CARDIOVASCULAR DISEASE AMONG DRAFTEES IN WORLD WARS I AND II Figures are based on Draft Board and Induction Station findings on the second million men in World War I and on men examined between April 1942 and December 1943 in World War II

overcrowding All such factors lower the resistance of the individual and predispose him to infection It is a common observation that more rheumatic patients come from poor families than from those of well to do people.

Age is an important factor Most of the cases have their initial involvement in childhood or early adolescence In the series of 488 cases of juvenile rheumatic carditis reported by Roth and co-workers,[7] the mean age of onset was 8 years. In the reports of Chang and Dieuaide,[8] including children and adults, 82 per cent had their onset before 30 years of age Leonard[9] feels that if a child escapes the disease up to fifteen years of age, he is likely to escape it entirely or will develop it in a less severe form. In his series of 500 cases, the initial attack generally developed between five

and eleven years. There are cases on record, however, where the disease occurred in early infancy and even in intrauterine life, as the one reported by Kissane and Koons,[10] as well as in advanced age. Green and Bennett[11] report a case where the initial attack occurred at 64 years and he quotes three other cases from the literature in the sixth and seventh decades of life The author has oberved two cases with initial attacks at 55 and 62 years respectively.

Sex is no important predisposing factor, appearing approximately with the same frequency in both sexes.

Climate is a definite factor influencing the occurrence of the disease It is more frequent in humid and cold regions in this country and the world

TABLE 11.—*Rheumatic Fever*

Geographic division	*Population (Est. 1944)*	*Mortality and rate per 1,000,000 population*			
		Acute rheumatic fever		*Chronic Rheumatic heart disease*	
		Mortality	*Rate*	*Mortality*	*Rate*
Continental United States	132,464,821	1,471	11 1	25,539	192 6
New England States	8,289,366	67	8 1	1,862	225 0
Middle Atlantic States	26,047,812	350	13 4	6,144	235 7
East North Central States	26,391,645	283	10 7	5,545	210.7
West North Central States	12,442,899	140	11 2	2,967	229 9
South Atlantic States	19,203,434	212	11 0	2,680	139 1
East South Central States	10,494,312	121	11 5	1,854	176 5
West South Central States	13,252,758	131	9 8	1,486	111 5
Mountain States	4,335,002	74	17 1	797	184 9
Pacific States	12,016,593	93	7 8	2,304	193 5

Death rate from acute rheumatic fever and chronic rheumatic heart disease in Continental United States and its geographic subdivisions, 1944

over, than in dry warm areas. It occurs more frequently in the north than in the south. In an examination of groups of school children in Indian reservations in Montana, Wyoming, New Mexico and Arizona, Paul and Dixon[12] found the incidence of rheumatic carditis to be ten times more frequent in the two northern states than in the southern Sharp and John[13] found the incidence of hospital admissions for rheumatic carditis to be 0 35 per cent for Chicago and 0 08 per cent for Galveston, Texas, a proportion of over 4:1. Chorea occurred about 33 times more often in Chicago than in Galveston. However, old rheumatic cardiovalvular disease was observed as frequently in both places.

In a study of the United States Vital Statistics Reports[1] on the mortality attributable to rheumatic fever and chronic rheumatic cardiovalvular dis-

ease in 1944, the author found the incidence of the latter to be definitely greater in the north than in the south and in the north eastern sea coast, than in the north east central states. The number of deaths from acute rheumatic fever did not always correspond to the number of deaths from chronic cardiovalvular disease in the same region Thus, in New England, the death rate from chronic cardiovalvular disease in relation to that of acute rheumatic fever, was proportionately much greater than in the mountain states. A summary is given in Table 11 This would indicate that a relatively greater number of cases who suffer from rheumatic fever in the north develops crippling cardiovalvular disease

Season The various reports from different parts of the world and the United States indicate that the greatest incidence occurs between September and June, during changeable weather, increased humidity, rain, snow, and cold In occasional reports, no definite seasonal incidence was noted

The Exciting Cause: The underlying exciting cause of rheumatic fever is not known In a great many cases, it is preceded by tonsillitis, pharyngitis, otitis media, and other infections one or two weeks prior to the onset of the disease Hence, some strains of streptococcus infection or their toxins were considered to be the cause of the disease by Clawson,[15] Coburn and Pauli[15] and other authors Although it is true that the incidence of respiratory infections in southern climates is lower than in the north and is greater in the winter than in the summer, which parallel the incidence of rheumatic fever, it has never been definitely proven that any of the streptococci is the underlying cause.

Weintraud[16] considered rheumatic fever an allergic disease In this country, Swift and co-workers[17, 18] advanced the theory that hypersensitivity to streptococcus infection is the underlying cause This theory is widely accepted today, although many believe that hypersensitivity to various other allergens may also produce rheumatic manifestations Pathologically, Clark and Kaplan[19] have demonstrated at autopsy inflammatory changes of the interstitial mesenchymatous tissue similar to that of rheumatic fever in cases of serum sickness More recently, Rich and Gregory[20] produced rheumatic lesions experimentally by anaphylactic hypersensitivity Clinically also, it is frequently observed, as pointed out by Bland and Jones,[21] that rheumatic fever may be precipitated by any factor which produces tissue destruction such as operative procedures, any forms of bodily injuries, vaccine injections, emotional crises and infections of all kinds, the most frequent being streptococcic It is possible also that chilling of the body surface by exposure to cold, damp weather produces vascular spasm resulting in ischemia of the affected part and microscopic destruction of tissues which may act as allergens in some cases.

Some authors believe that a filtrable virus may be the underlying exciting

cause of the disease. Schlesinger and co-workers[22] obtained minute bodies resembling virus particles on high speed centrifugation of pericardial fluid from cases of rheumatic fever These were agglutinated by serums from cases of acute rheumatic fever but not from non-rheumatic disease. They believe that streptococcus infection in some way activates this virus More recently, MacNeal and co-workers[23] have reproduced typical rheumatic *lesions in animals by injecting a bacteriologically sterile filtrate from peri-*



FIG 107—ACUTE RHEUMATIC MYOCARDITIS Many Aschoff bodies are seen, most of them coalescing × 30

cardial fluid of a patient who died from rheumatic carditis. Propagating this serum by blood transfusion in rabbits and in embryonated eggs, and injecting it intravenously, produced more pronounced lesions Injection of normal human serum, vaccine or influenzal virus produced no identical lesions. They therefore, considered that the disease is produced by a *specific virus.*

Rinehart[24] believes that deficiency in vitamin C, and Shank and co-

workers[25] think that deficiency in vitamin A may partly be responsible for the disease.

PATHOLOGY

The characteristic active rheumatic lesion is the *Aschoff body or submiliary nodule* It consists of a central area of swollen, fragmented and necrotic collagen surrounded by *Aschoff cells*, lymphocytes, *plasma cells* and occasionally polymorphonuclear cells as well as some fibroblastic proliferation The Aschoff cells are peculiar, large endothelial cells with abundant granular cytoplasm and contain one or more nuclei and prominent nucleoli Figures 107 and 108 show the Aschoff bodies



FIG 108 — ASCHOFF BODY, HIGHER MAGNIFICATION THAN IN FIG 107 Swollen disorganized collagen surrounded by cells of variable shapes Many of the cells have dark staining cytoplasms, more than one nuclei and prominent nucleoli × 80

The size of the Aschoff body varies greatly from a few cells seen under the microscope to a collection large enough to be seen with the naked eye They always develop in the mesenchymal or interstitial tissue of an organ or structure, usually close to a small blood vessel They are most frequently found in the myocardium close to the adventitia of the small branches of the coronary arteries where they are usually elongated or lemon-shaped

There are other inflammatory changes in rheumatic fever affecting the mesenchymal tissue which are far more extensive and widespread than the Aschoff bodies Von Glahn and Pappenheimer[26] described a panarteritis involving the aorta and various other arteries throughout the body. The involved artery is characterized by a thickening of its wall due to the formation of fibrin and fibrosis of the cellular elements Surrounding the affected vessel, there is a loose fibrillar stroma in which are many kinds of cells, some with large vesicular nuclei which are distinctive Vascularization of the vessel wall by the formation of new capillaries takes place so that the original lumen becomes surrounded by a spongy vascular tissue

The Heart

Pathologic changes here affect the endocardium, myocardium, and pericardium in different degrees in various cases These consist of acute inflammatory changes and various degrees of Aschoff body infiltration, which if mild and nonprogressive, may clear and leave no trace. If more severe and progressive, they may lead to organized fibrosis, scarification and even some calcification These result in permanent valvular deformities, fibrosis of the heart muscle and pericardial fibrosis and adhesions in various degrees

From a pathologic viewpoint, we recognize an ***active acute phase*** very early in the disease, with no fibrotic changes, ***a chronic active phase*** where concomitant with reparative or fibrosing processes in some parts of the heart, fresh acute involvement occurs in other parts, and a ***healed*** or ***inactive phase*** where no acute lesions are found, the pathologic processes consisting merely of an organized fibrosis

Endocarditis and Valvulitis: In the acute phases, the affected valves, mainly the mitral and aortic, more rarely the tricuspid and pulmonic, become edematous due to inflammatory changes There is marked cellular infiltration, swelling of collagen and an occasional Aschoff body. On the endocardial covering of the valves small, wartlike vegetations develop along the lines of closure of the leaflets which may be seen with the naked eye They may reach 3 millimeters in height They are pale grayish, or yellowish in color and are firmly adherent They may also occur on the chordae tendineae. Increased vascularity of the valves occurs

In the healed inactive phase, the process is replaced by fibrous connective tissue which results in more or less stiffening, fusion and thus stenosis of the mitral and tricuspid valve leaflets. The semilunar valve leaflets may be shortened, retracted and adherent to each other, resulting in insufficiency and stenosis Shortening, thickening and matting together of the chordæ tendineæ may occur producing retraction of the mitral and tricuspid leaflets and insufficiency of these valves.

The mural endocardium, especially that of the left auricle, may also undergo inflammatory changes resulting in thickening and fibrosis

Myocarditis: The inflammation here is interstitial and is characterized by an abundance of Aschoff bodies, as said before. If not extensive and progressive the process may absorb, leaving no residue If progressive and severe, replacement interstitial fibrosis of the myocardium takes place

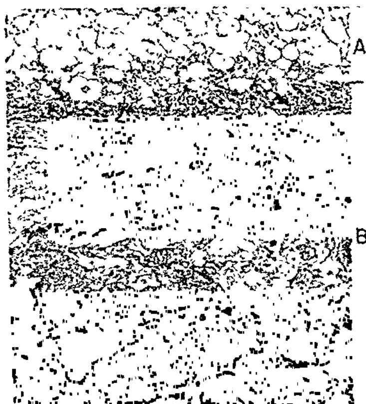


FIG 109—RHEUMATIC PERICARDITIS Section of the parietal pericardium, showing A, pericardial fat, B, exudative inflammation with enmeshed desquamated mesothelium, indicated by arrows Considerable vascular distention is noted with some hemorrhage × 80

resulting in permanent damage By the nature of the acute lesions, the fibrosis is patchy rather than diffuse

Pericarditis: In the acute stage, the gross appearance of the pericardium, if inflammation is extensive, is characterized by yellowish fibrin covering the surfaces of the pericardium and more or less accumulation of pericardial effusion, usually serous but occasionally serosanguinous. In mild cases, the pericardial surface merely becomes lusterless without any fibrin covering

it Microscopically, Aschoff bodies are rarely found in the pericardium. The endothelial cells beneath the fibrin are swollen and in places denuded. The connective tissue beneath the endothelium is edematous and is infiltrated with large mononuclear and polymorphonuclear cells and lymphocytes. Many new capillaries and small blood vessels develop, some of which bleed Fibroblastic changes may be observed in some places in the more chronic cases See Figures 109 and 110

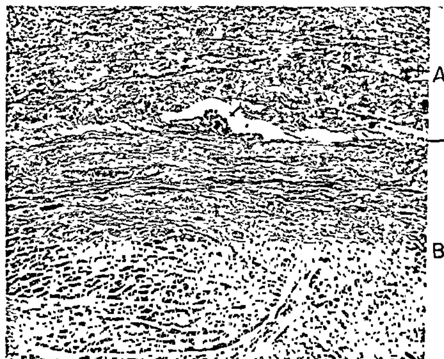


FIG 110—RHEUMATIC PERICARDITIS Section of the visceral pericardium showing A, exudative inflammation with enmeshed groups of proliferative mesothelium of the epicardial lining, indicated by arrow The subjacent myocardium, B, shows active inflammation with many dilated arterioles and capillaries × 80

In the healed phase, pericardial adhesions may be present in various degrees or there may be merely thickening of the visceral pericardium.

Aortitis and coronary arteritis may be extensive and is of the nature described in other arteries of the body by Von Glahn and Pappenheimer

Changes in Other Organs: Pneumonitis and pleurisy occur fairly frequently in rheumatic fever. Recently, Griffith and co-workers[17] reviewed the literature of pleuropulmonary involvement in rheumatic fever and reported a pathologic study of 119 cases of their own. Grossly, the lungs are mottled

Microscopically, angiitis of large vessels and capillaries was observed as in anaphylaxis. Hemorrhage, necrotic changes, cellular infiltration and Aschoff bodies were seen. Alveoli were filled with fibrin, collagen and blood cells. Serofibrinous pleural exudate occurred and pleural adhesions were noticed at times.

Cerebral involvement may occur and may consist, in the acute phase, of nonsuppurative meningo-encephalitis, described by Whitelman and Eckel.[28] Late cerebral sequelæ in the form of obliterating endarteritis of small meningeal and cortical vessels were described by Bruetsch.[29] This may occur in patients otherwise in good health, and results in gross and microscopic infarction of some of the gray matter. Cerebral embolization from mural thrombi in the heart is another late manifestation.

Renal involvement has been observed by Goldring and Wyckoff[30] and by Coburn.[31] The latter considered hematuria a classic sign of active rheumatic infection comparable to nosebleed.

Clinical Manifestations

These vary in their mode of onset, symptomatology and progress, depending upon the rapidity and extent of development of the pathologic processes and the organs which are predominantly affected, as discussed in a previous communication.[32]

Modes of Onset and Course

In many cases, the onset of the disease is very insidious. It frequently follows an upper respiratory infection. The patient develops a tired feeling towards the later part of the day, an occasional ache or pain in various parts of the body, loss of appetite and often a nervous and irritable state. As time goes on, progressive pallor develops together with loss of weight and weakness. The pulse rate is found to be accelerated above normal and there is an occasional rise in temperature as high as 101 or 102 degrees F towards evening. These symptoms may soon become more severe. A skin eruption and epistaxis may occur from time to time. Occasional pain in the chest may be present, especially in the precordial region. Subcutaneous nodes may be detected. The heart is found to be accelerated far above that expected with the given temperature and abnormalities in sounds as well as murmurs may occur. Prolonged bed rest and proper therapy may result in gradual recession of symptoms and recovery may take place with or without gross residual heart damage.

In other cases, the onset of the disease is more abrupt. One or two weeks after an attack of scarlet fever or severe tonsillitis, pharyngitis, bronchitis, middle ear disease or other infection, the patient may suddenly develop swelling, tenderness, redness and severe pain in a joint such as an ankle or

knee with rise in temperature, rapid heart rate, sweating, restlessness and marked irritability Soon other joints become involved and the pain may at times become unbearable The joints that were involved early, may improve while others are affected In the rare fulminating form, the temperature may rise very high, marked leukocytosis may develop, severe involvement of the heart and other organs may ensue and death may result in a few days to several months In the milder forms, recovery may take place after many months with residual cardiac damage

Both the insidious and abrupt forms of acute rheumatic fever may recur every few years or sooner, with freedom from symptoms between attacks. In some cases, the process is continuous in a subacute or chronic form for years with progressive diminution in cardiac reserve, marked fatigue, progressive anemia and low grade temperature The variations in the clinical manifestations of rheumatic fever have thus been classified by Swift[33] into *monocyclic, polycyclic and continuous*

In a study of the records of 499 cases of rheumatic fever, Wilson and Lubschetz[34] found that in individuals between 4 and 13 years of age, 25 per cent of cases had recurrences Between 14 and 16 years, the recurrence rate was 8.6 per cent and between 17 and 25 years of age only 3 7 per cent The over all risk for a major recurrence is 2 to 3 times greater in the year following an attack than later

Localization of Involvement

It will be seen from the above symptomatology that the manifestations of rheumatic fever are protean in nature In many cases, however, the predominant manifestations are localized to given structures or organs It is essential, therefore, to have a clear idea of such localization to help in our diagnosis and to avoid misdiagnosis We shall review here some of the characteristics

Joint Involvement: This may occur in about 50 per cent of all cases. It may be very mild or severe The latter occurs more frequently in adults. As said before, it is characterized by its migratory nature. If the given joint is severely involved, it is hot, painful, tender, red and swollen. Usually, the pain is slight and stiffness may be the prominent feature We must bear in mind the fact that in rare cases, involvement of the spinal joints may take place resulting in stiffness of the neck which together with the fever and leukocytosis may simulate meningitis.

Muscular Involvement· This occurs perhaps as frequently as joint involvement. It is characterized by aches, pains and stiffness or localized contractures of given groups of muscles. Torticollis is an outstanding example. The so-called "growing pains" may be the outstanding symptom of the disease in childhood.

Subcutaneous Nodes: These, if present, are characteristic manifestations of active rheumatic fever. They are proliferative lesions which may be overlooked. They usually appear in crops over bony prominences, tendons and joints They are not painful or tender and are freely movable They are firm and elastic in consistency and vary in size from a pinhead to a lima bean They may last a few days to several months and may recur for months or years in an occasional chronically active case

Skin Involvement: This occurs in about 4 to 10 per cent of rheumatic cases. The more common manifestations are fine papular eruptions, erythema multiforme, marginatun and annulare. Erythema nodosum and purpuric eruptions occasionally occur Urticaria may also be observed in occasional cases.

The various eruptions usually appear in the active phase of rheumatic fever, although they may first be observed at recovery They are usually transitory

Acute and Recurring Nephritis: In occasional cases, renal involvement is a conspicuous manifestation. However, it is seldom severe. It must be borne in mind that albuminuria and hematuria which are important criteria in the diagnosis of nephritis may result from the administration of salicylates.

Abdominal Involvement: This is characterized by a gradual or sudden onset of diffuse abdominal pain which may soon localize to one of the upper or lower quadrants and may be accompanied by vomiting, local tenderness, rigidity and leukocytosis The condition may simulate appendicitis or other acute abdominal disease. Many of the reported cases have been erroneously operated on.

Nervous System Involvement Here, *chorea* is the outstanding manifestation in childhood and adolescence The severe form can be easily recognized by the characteristic incoordinated movements of various muscle groups of the body The mild forms may be overlooked unless the patient is carefully observed There is merely an occasional slight movement of an arm or intermittent twitch of a muscle, together with some restlessness

Other and rarer manifestations of cerebral involvement, especially in adults, may occur in the acute phase or during convalescence Warren and Choryak[35] report five cases of rheumatic encephalitis presenting hallucinations, various phobias, panic-like episodes, delirum, restlessness, mask-like facies and in some, even convulsions. They cite cases from the literature where the diagnosis of schizophrenia was made, as the cerebral symptoms may occur with little or no joint involvement

In milder cases, there may merely be restlessness, and the patient may complain of headache Ménière's syndrome has been rarely observed, and rheumatic meningitis has been described

Respiratory Involvement. This is characterized by pleurisy, usually with effusion and a migrating pneumonia. Localized chest pain, pleural friction rub and hemoptysis may or may not be present

Cardiac Involvement

The percentage of rheumatic fever cases that develop carditis varies in different reports. Coombs[36] places it at 75 per cent. These are also the approximate figures given by other authors Jones and Bland,[37] in a study of 1,000 cases of rheumatic fever and chorea, found an incidence of 80 per cent Ash,[38] on the other hand, found an incidence of 59.2 per cent of cardiac involvement at the termination of the initial attack in a series of 547 children It is very likely that a much greater percentage, and perhaps all cases of rheumatic fever have some cardiac involvement, which does not reach the clinically recognizable stage

The tragedy of heart involvement in rheumatic fever is that in Nature's attempt at repair of the inflammatory processes, it leaves this organ in a scarified and permanently diseased state This is true, to some extent of the other organs, in severe cases The heart, however, is far more frequently and more extensively involved, and it shows a greater tendency to proliferative changes and cicatrization What is more important, abnormalities in the heart function caused by the pathologic changes produce greater interference with the general economy and welfare to the human organism than similar disturbances of other organs

The clinical, like the pathologic manifestations of rheumatic heart disease may be divided into those of the *active acute phase* the *chronic active phase* and the *healed inactive phase.* In each of these phases, the degree of cardiac damage, the general constitutional state of the patient and the extent of rheumatic involvement of other parts of the body determine the symptomatology

The Active Acute Phase In the early period, there are no symptoms referable to the heart except simple tachycardia, which is common to all acute disease The heart rate here, however, is usually far out of proportion to the rise in temperature Aside from the tachycardia, acute rheumatic carditis may go for weeks or months without being recognized, especially if no other active rheumatic manifestations are present. Frequently, a transient recurring systolic murmur may be heard in different parts of the precordium which may be due to the tachycardia and to the anemia, although inflammatory edema of the valves and some dilatation of the left heart chambers must be considered when such murmurs appear.

As the pathologic process progresses, the patient may begin to experience some precordial pain which at times becomes increasingly severe Pain occurs more frequently after repeated attacks of carditis. It may often be

used as an index of the development of permanent valvular damage It is usually in the form of a persistent dull ache in the precordial region It may, however, be intermittent and sharp, especially in the presence of pericarditis. If the adjacent pleura is involved, it may become more marked on deep breathing The patient may also experience some palpitation from time to time, slight dyspnea and precordial discomfort.

Objectively, if the heart is greatly involved, especially in the presence of severe myocardial damage, it may undergo progressive increase in size and show changes in the character of the heart sounds, becoming somewhat muffled, split, reduplicated, and a gallop rhythm may develop These abnormalities may be due partly to progressive increase in valvular pathology and its effect on the hemodynamics and partly to the myocardial disease Various disturbances in the rhythm may occur from time to time. If considerable pericarditis is present, a localized or diffuse pericardial friction rub may develop This is an infrequent occurrence and is observed more often in children than adults In severe cases, massive pericardial effusion accumulates and produces dyspnea and other manifestations which are fully described in Chapter XXV

The electrocardiogram is often of great diagnostic importance in acute myocardial and pericardial involvement Transient and intermittent prolongation of the PR conduction time and frequent changes in the initial and terminal ventricular complexes are often observed These have been fully described elsewhere.[39]

Endocarditis and valvulitis occur most frequently and the mitral valve is the one most commonly involved In 109 autopsy cases of rheumatic heart disease, Pappenheimer and Von Glahn[40] found the mitral valve to be involved in 90 8 per cent, the aortic valve in 57 7 per cent, the tricuspid valve in 41 3 per cent and the pulmonic valve in 3 3 per cent Pericarditis was found in 37 5 per cent These figures apply, of course, to fatal cases and to pathologic findings In nonfatal cases, involvement of the tricuspid and pulmonic valves are comparatively rare or are present in a degree which is not clinically demonstrable

Mitral valve damage may exhibit itself early by a transient systolic murmur heard along the left sternal border due to edema of the leaflets. Later, when insufficiency develops, the murmur moves to the more classic location at the apex and assumes the characteristic transmission to the left axillary region At this stage, most cases show also a very short, mid-diastolic rumble or an accentuated third heart sound at the apex, characteristic of the onset of mitral stenosis This usually occurs several months after the onset of the disease.

Involvement of the aortic valve may be suspected with the development of a systolic murmur at the aortic area. The characteristic rough, systolic murmur with its usual transmission heard in advanced aortic stenosis,

however, is not present in early aortic valvulitis This murmur in acute aortic valvulitis is of much lower intensity, is more localized and tends to change in quality from time to time. Although the murmur is highly suggestive of aortic valvulitis, it cannot be taken as a definite indication of this condition until the soft diastolic murmur of aortic insufficiency appears in the aortic area or in the third left intercostal space with the characteristics described in Chapters IX and XXIV.

The Chronic Active Phase: In this form of rheumatic heart disease, a variable degree of activity may be demonstrated clinically which persists for many months and in some cases years The activity usually occurs stealthily and unless the patient is carefully observed, may be easily overlooked Often we must resort to rheumatic manifestations in other parts of the body to assume that whatever cardiac symptoms the patient presents are due to active cardiac changes

The subjective manifestations may be recurring precordial pain and palpitation, progressively increasing dyspnea and other signs of cardiac failure

Objectively, the various arrhythmias may be observed from time to time A progressive increase in valvular damage may be demonstrated as time goes on by the intensification and increase in the number of murmurs and by increase in the size of the heart. The constitutional signs of activity such as general body aches and pains, low grade fever, rapid heart rate, leukocytosis and increased sedimentation rate may be demonstrable. It must be remembered that many of these patients may show these signs of activity only intermittently For this reason, a careful follow-up for many months is essential

In some cases, there may be periods of months or years when the patient is apparently symptom free followed by periods of acute severe exacerbations These exacerbations may be precipitated by some infection in any part of the body, some operation or bodily injury. The author has noted some recurrences during and after pregnancies As an example, he recently observed a patient who had moderately advanced mitral stenosis for many years with evidence of slight recurring cardiac reactivation from time to time After a second pregnancy, she had recurring precordial pain and palpitation, occasional cough and recurring very low grade fever over a period of six months. At the end of that time, definite evidence of some aortic insufficiency was noted in addition to mitral stenosis, indicating that active valvulitis was taking place

The onset of gradual and progressive congestive failure in a previously well compensated case of chronic valvular disease may indicate that acute rheumatic reactivation of the heart is taking place. We must rule out, however, such conditions as heart strain due to overwork or to the various

tachycardias and arrhythmias, if present, which may cause heart failure. We must also rule out gradual onset of coronary sclerosis as a possible cause

The Chronic Inactive Phase: Here, organized valvular, myocardial or pericardial involvement has reached a given stage of development without further reactivation over a period of years.

The symptomatology in these cases depends upon the extent of cardiac damage, the strain under which the heart is working by virtue of the patient's occupation and the sensitivity of the individual. Many cases, even with a marked degree of valvular pathology may carry on a considerable amount of activity for many years without undue discomfort. In fact, in some cases, the patient is not aware of the existence of heart disease until he is told of the condition by an examining physician. As a rule, however, cases with marked degrees of valvular disease, myocardial damage or pericardial involvement cannot carry on the same amount of work as a normal individual Any extra strain thrown on the heart results in some dyspnea and, at times, precordial pain. The latter symptom may occur especially in the presence of aortic stenosis and insufficiency. Here, some cases may exhibit the typical anginal syndrome, as described in Chapter XIV, which may be relieved by nitroglycerine.

Although no progression of the rheumatic cardiac lesions occurs in these cases, various physiologic disturbances in rate and rhythm, described in Chapter VII, may occur here more frequently than in normal persons. This is true particularly of mitral stenosis where auricular fibrillation develops sooner or later in the majority of cases if the patient lives long enough. In a study of the records of 3,129 cases of rheumatic fever and carditis from the affiliated heart clinics of the New York Heart Association, from the onset of the disease to death, Cohn and Lingg[41] found that the longer the life of the individual with heart disease the more likely is auricular fibrillation to occur. The arrhythmia occurred in only 20 per cent of cases who lived less than four years and in 72 per cent of those who lived longer than thirty years

The subjects of chronic valvular, chronic myocardial and pericardial involvement will be discussed in Chapters XXIV, XXV and XXVI

Differential Diagnosis

The acute and subacute phases of rheumatic fever may often be mistaken for other diseases that may have the same clinical features. Inasmuch as we have no specific bacteriologic or serologic tests for rheumatic fever, we must depend entirely upon the clinical findings and upon some laboratory tests that may be specific for the other diseases, for our differential diagnosis.

Cases with Arthritic Manifestations: These may be confused in the early

phases with acute infectious arthritis, early stages of gout, osteomyelitis, localized near a joint, puerperal sepsis, postscarlatinal arthritis and serum sickness. The outstanding differential diagnostic features of rheumatic arthritis are the migratory nature of the joint involvement and its response to salicylates

In acute multiple infectious arthritis, the joint involvement is not migratory and the affected joints are more acutely inflamed The synovial fluid is purulent and infectious organisms may often be demonstrated There may also be a history of recent purulent tonsillitis, cerebro-spinal meningitis and so on

Acute gout is easily ruled out by the location of the affected joints, the occurrence of tophi, the characteristic x-ray findings and high uric acid in the blood

Osteomyelitis near a joint is ruled out by the septic temperature, chills, profound intoxication, marked leukocytosis and x-ray findings

Puerperal sepsis, scarlet fever and serum sickness arthritis are ruled out by the history

Cases with Visceral and Septic Manifestations These must be differentiated in the early phases from subacute bacterial endocarditis, undulant fever, typhoid or paratyphoid fever, an acute surgical abdominal condition, pulmonary tuberculosis, pleurisy, pneumonia and other conditions discussed before

Subacute bacterial endocarditis usually occurs in cases of pre-existing valvular disease and is characterized in many cases by embolization, splenic enlargement and positive blood cultures, as will be described in the following chapter

Undulant fever may be recognized by a positive blood agglutination test for Brucella melitensis *Typhoid infections* may be recognized by stool and blood cultures and later by the Widal reaction.

The localized manifestations of the disease may in rare cases offer difficulty in differential diagnosis early in the disease, especially where an acute surgical abdominal condition is simulated In some of these cases, operation will reveal an erroneous diagnosis and the future course, including cardiac involvement will reveal the true nature of the disease

Prognosis

There are many factors that influence the prognosis in rheumatic fever and rheumatic heart disease The most important are the severity of the acute phase, the age at onset, its duration, the frequency of its recurrence and the extent of cardiac involvement These are governed to a great extent by the constitutional state of the patient, the care he receives, his financial and environmental status, the type of work he has to do after re-

covery and the exposures to inclement weather, physical and mental strain and infections

In the series of 3,129 fatal cases of rheumatic heart disease reported by Cohn and Lingg,[41] it was observed that in those cases where the early manifestations were mild, the subsequent course was usually mild. If it began in a severe form in childhood, 80 per cent died before the end of adolescence.

The age at onset of the disease is one of the most important prognostic factors. In this series two thirds had their onset in childhood. Of these *only 5 per cent survived to the age of 46 years or over.* One-third of these did not live beyond childhood, another third did not live beyond 20 years. Most of the cases who first developed the disease in adolescence, however, lived a fairly long life, even to advanced age. Taking the entire series as a whole, 10 per cent lived more than 30 years, 25 per cent more than 17 years and 50 per cent as long as 9 years. The over-all average life was 13

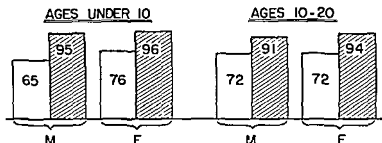


FIG 111 —PERCENTAGE INCIDENCE OF SURVIVAL IN A FOLLOW-UP OF ABOUT 3000 CHILDREN WITH RHEUMATIC HEART DISEASE OVER A PERIOD OF EIGHT YEARS. Metropolitan Life Insurance Company, Industrial Department. M, males, F, females. White area indicates heart involvement, shaded area no heart involvement

years. The shorter the attack, the better the prognosis. Long attacks and frequent recurrences have a poor prognosis

The extent of cardiac involvement is the most important factor governing the prognosis. Thus, taking the onset of auricular fibrillation as an index of the extent of cardiac disease in the rheumatic group, we find in the Cohn and Lingg series that only 10 per cent survived three years from its onset if this arrhythmia developed in childhood. If it began in adolescence, 10 per cent survived four years, if after twenty 10 per cent survived seven years.

In a series of about 3,000 children with rheumatic fever followed for eight years by the Metropolitan Life Insurance Company, however, the great majority survived at the end of that period, as shown in Figure 111. The greatest incidence of survival was among those who had no demonstrable heart involvement.

The effect of cardiac involvement on longevity and on the mortality rate from rheumatic fever is well illustrated in the report by Ash.[35] He followed up a series of 547 rheumatic children for a period of ten years after the initial attack. Of 219 patients in this group who showed no evidence of heart disease, only 5 per cent died of rheumatic infection or bacterial endocarditis On the other hand, of 318 patients with heart involvement 42.1 per cent died of such conditions.

The mode of death in rheumatic fever varies with the stage of the disease when it occurs. In general, about 80 per cent to 90 per cent of cases die from some form of cardiac involvement. In the series of 306 fatal cases in young persons reported by Bland and Jones,[42] 8 per cent died of acute rheumatic fever; 67 per cent of acute rheumatic fever with congestive failure, 7 per cent of congestive failure alone; 6 per cent of bacterial endocarditis, 3 per cent of other heart disease, 5 per cent of causes unrelated to the heart and 4 per cent of unknown cause. In a series of 100 autopsy cases of rheumatic heart disease in adults, Juca and White[43] found that 35 per cent died in congestive failure without rheumatic reactivation; 22 per cent of congestive failure with reactivation; 18 per cent of bacterial endocarditis and 14 per cent of other causes related to the heart such as myocardial infarction and embolization Eight died of causes unrelated to the heart.

Treatment

The primary aim in the management of this devastating disease is to prevent its occurrence. When the disease develops, the indications are to render symptomatic relief and to minimize its destructive effects on the heart and other parts of the body.

Preventive Measures

The long range preventive measures should include, perhaps, not only the control of the environmental conditions, but also of the hereditary factor.

The Control of the Hereditary Factor: Although it has not been definitely established that heredity plays a part in the predisposition to this disease, *there is suspicion that it does. It is, therefore, advisable to discourage* marriage among individuals where there is strong tendency to rheumatic disease in the respective families. Where marriage has taken place, the question of childbearing should be weighed very carefully. This is particularly true where chronic rheumatic heart disease is present in one or both of the married pair. In such cases, not only a possible hereditary transmission of the given constitutional predisposition to the future offspring is to be considered, but also the effect of its environmental contact with the rheumatic parents. Although contagion is probably nonexistent in the inactive phase of the disease, one can never tell when reactivation may occur.

The Control of Environmental Factors: This includes the removal, if possible, of all factors which are known to predispose to the disease This is true, especially for individuals who have a tendency to the disease. A well-balanced nutritious diet, the avoidance of exposure to inclement weather, the use of proper clothing, general cleanliness, fresh air and sunshine are essential Exposure to infections of all kinds should be avoided.

The Use of Prophylactic Drugs: Within the past few years, the literature has recorded favorable response in the reduction in the incidence of acute rheumatic fever by the prophylactic use of sulfadiazine in dosage of 0 5 gram twice daily Thus Holbrook[44] found a reduction of 50 to 75 per cent in the incidence of respiratory disease and streptococcus infections by the use of these drugs in the army. He also observed that the reduction in the incidence of rheumatic fever paralleled that of the respiratory and the streptococcus infections The same observations were reported by Fullerton[45] among 250,000 sailors who were given these drugs during the winter months This author found that the incidence of scarlet fever and meningococcus meningitis was also greatly diminished by the prophylactic use of the sulfa drugs Wolf and co-workers[46] observed that in 70 rheumatic children there was no acute recurrence of the disease for two years while sulfathiazole or sulfadiazine was used as a prophylactic measure.

It would seem from these reports that the sulfa drugs may be of value in the prevention of acute rheumatic fever in individuals who have a predisposition to the disease. These drugs, however, have no place in the treatment of the disease when it already exists

Tonsillectomy as a Prophylactic Measure: The question as to whether tonsillectomy is of any value in the prevention of rheumatic fever or the recurrence of an acute exacerbation has never been answered satisfactorily. Kaiser[47] observed 48,000 school children for five years or more. In 20,000 who had had tonsillectomies, the incidence of rheumatic fever was 8 per cent In 28,000 whose tonsils had not been removed the incidence was 10 per cent Thus, tonsillectomy appears to offer protection against the development of rheumatic fever in 2 per cent of cases On the other hand, the incidence of carditis following chorea as well as the frequency of valvular disease was decidedly less in tonsillectomized children. Also, the incidence of scarlet fever was twice as frequent in children whose tonsils had not been removed.

Roby and Finland[48] observed excellent results from tonsillectomy in some cases They feel that it may be performed even during the active stage of rheumatic fever, if necessary.

The author feels that tonsillectomy may be of value only in those cases where the tonsils are definitely infected or where they are so large as to obstruct breathing The promiscuous sacrifice of tonsils on the theory that they may serve as foci of infection is unjustifiable

Treatment of the Acute Phase

Bed Rest During an acute episode of rheumatic fever absolute bed rest is generally considered to be the most important part of therapy. This should be strictly enforced until all signs of activity subside, regardless of the length of time it takes This means that bed rest is to be enforced until the temperature, pulse rate, blood count and the sedimentation rate come down to normal values and remain continually normal at least two weeks, and until the patient becomes asymptomatic If any signs of activity recur, further bed rest should be continued. The length of time bed rest is to be continued depends upon the severity and course of the disease. It may vary from a few weeks to many months.

Recently, Robertson and co-workers[49] suggested that the present treatment of prolonged bed rest in this disease be re-evaluated. Based on the observation of 200 cases they concluded that patients with no complications who show rapid recovery do not require prolonged bed rest, and that such rest predisposes to a high incidence of anxiety neurosis. This is true in those cases where we are convinced that there are no cardiac complications, and where the recovery is complete Those cases that show evidence *of some activity should be kept in bed, like cases of active tuberculosis,* until all signs of activity subside We often see cases which show signs of valvular disease months or years after an apparently insignificant attack of rheumatic fever. Evidently, some low grade smoldering inflammation has been going on stealthily.

Diet There is no particular type of food necessary in this disease. The old idea that a high protein diet is harmful has been definitely disproved by Thompson and Edgar[50] as well as by other authors The only rule is to give a high caloric diet, enough to help raise the resistance, replace wear and tear, and to supply the necessary amount of material for growth. Large amounts of the vitamins may be of added value.

Salicylate Therapy. The value of the salicylates in the therapy of rheumatic fever is still controversial. That it has a specific effect as an analgesic and as such is of great value in those cases where the main presenting symptom is joint or muscular pain, is generally acknowledged. It is also agreed that it has an antipyretic effect Whether or not it has any specific effect in shortening the course of the disease or in preventing the development of carditis, however, has not been definitely proved. Manchester[51] agrees with Coburn that intensive salicylate therapy in doses of 10 to 16 grams per day suppresses rheumatic infection, prevents toxic manifestations, and has an effect in diminishing cardiac involvement. Warren and co-workers,[52] on the other hand, found that massive doses of 10 to 16 grams per day may help relieve the early symptoms and reduce the temperature, but does not prevent cardiac involvement. Furthermore, Wégria and Smull[53] found that an adequately treated group of patients with a serum salicy-

late blood level, of 350 to 500 micrograms, as advised by Coburn showed no shorter course than a group treated with smaller doses, having a serum salicylate level of 250 micrograms. These were also the observations of Keith and Ross.[54] That salicylate therapy does not suppress the inflammatory reaction was shown by Harris,[55] who found no diminution of clinical activity or in the leukocytic count under massive salicylate therapy, although the sedimentation rate was lowered.

My personal experience has been that the salicylates are excellent adjuncts in the therapy of rheumatic fever in relieving pain, in lowering the temperature, and in keeping the patient more comfortable I am not convinced, however, that the duration of the disease is shortened by these drugs, nor that they prevent or diminish cardiac involvement In fact, they are occasionally misleading in giving us a false sense of security because they diminish the symptoms

The dosage used depends upon the severity of symptoms, the height of the temperature, as well as the age of the patient. It varies between 60 and 200 grains per twenty-four hours, given in divided doses There is no advantage in adding sodium bicarbonate to the therapy. In fact, Smull and co-workers[56] showed that it is disadvantageous to add this drug

Toxic effects of salicylates have been recorded by various observers. Erganian and co-workers[57] observed listlessness, hyperpnea, fever, epistaxis, tarry stools, xanthochromia, muscular twitching and convulsions as toxic manifestations in infancy and childhood

Other Therapeutic Measures: Where the joint pain is extremely severe, immobilization is necessary by proper splints well padded with cotton. The application of oil of wintergreen may be of help. Codeine sulphate in doses of ½ to 1 grain may, at times, be necessary to give relief.

Amidopyrin in doses of 5 to 10 grains, often repeated, may give more relief in some of these cases than the salicylates Both codeine and amidopyrin may be given together with the salicylates in some cases to get the synergistic effects The dosage for children is to be regulated according to age.

Period of Convalescence

The convalescence from an acute episode calls for prolonged rest and relaxation, preferably in some healthful country place Plenty of fresh air, sunshine, and good nutrition are necessary to increase the resistance of the patient A frequent follow-up is very essential to determine from time to time if there is evidence of reactivation

The return to active life should be slow The type of activity to be allowed is to be gauged by the degree of cardiac damage, if any is present, and particularly by the functional capacity of the heart, as discussed in Chapter XIII.

REFERENCES

[1] Vital Statistics Special Reports, U S Dept of Commerce, Bureau of Census Vol 25, No 6, June 26, 1946
[2] Wyckoff, J, and Lingg, C Statistical studies bearing on problems of classification of heart disease Am Heart J 1 446, 1926
[3] Cahan, J M · Rheumatic heart disease in Philadelphia school children Ann Int Med 10 1752, 1937
[4] Swift, H F, and McEwen, C Rheumatic fever Oxford Med 5 11, 1938
[5] Wilson, M. G Rheumatic Fever New York, The Commonwealth Fund, Division of Publications, 1940
[6] Griffith, G C, Moore, F J, McGinn, S, and Cosby, R S · The familial incidence of rheumatic fever Am Heart J 35 438 and 444, 1948
[7] Roth, I R, Lingg, C, and Whittemore, A Heart disease in children Am Heart J 13 36, 1937
[8] Chang, F C, and Dieuaide, F R A clinical study of rheumatic fever Chinese M. J 51 581, 1937
[9] Leonard, M Puberty and prognosis in rheumatic fever Am Heart J 14 192, 1937
[10] Kissane, R W, and Koons, R A Intra-uterine rheumatic heart disease Arch Int Med. 52 905, 1933
[11] Greene, J A, and Bennett, A W: Acute rheumatic heart disease in the aged with report of case with Stokes-Adams syndrome treated with paredrine Am. Heart J 30.415, 1945.
[12] Paul, J R, and Dixon, G L · Climate and rheumatic heart disease A survey among American Indian school children in northern and southern localities J A M A 108 2096, 1937
[13] Sharp, W B, and John, M B Climate and the streptococcus rheumatism relationship. J Infect Dis 60 15, 1937
[14] Clawson, B J Experimental subcutaneous rheumatic nodules Am J Path 4 565, 1938, Bacteriology of acute rheumatic fever Minnesota Med 14 1, 1931
[15] Coburn, A F, and Pauli, R H Studies on the relationship of strep hemolyticus to the rheumatic process J Exper Med 56 609, 1932, J Clin Investigation 14 783, 1935.
[16] Weintraud, W. Der Akute Gelenkrheumatissmus Part 2, 133 Berlin, Kraus-Brugsh, 1919
[17] Swift, H F, Hitchcock, C H, Derick, C L., and McEwen, C Intravenous vaccination with streptococci in rheumatic fever Am J M Sc 181 1, 1931
[18] ——, Derick, C L, and Hitchcock, C H Intravenous vaccination with strep. Am J Phys. 43 192, 1938
[19] Clark, E, and Kaplan, B. I Endocardial, arterial and other mesenchymal alterations associated with serum disease in man Arch Path 24 458, 1937
[20] Rich, A R, and Gregory, J E On the anaphylactic nature of rheumatic pneumonitis Bull Johns Hopkins Hosp 73 465, 1943, Further experimental cardiac lesions of the rheumatic type produced by anaphylactic hypersensitivity Bull Johns Hopkins Hosp 75:115, 1944
[21] Bland, E F, and Jones, T D. Clinical observations on the events preceding the appearance of rheumatic fever J Clin Investigation 14 633, 1935
[22] Schlesinger, B, Signy, A G, and Amies, C R Etiology of acute rheumatism Experimental evidence of a virus as the causal agent Lancet 1 1145, 1935
[23] MacNeal, W J, Blevins, A, Slavkin, A E, and Scanlon, H Experimental verrucous endocarditis Science 101.415, 1945
[24] Rinehart, J F Studies relating vitamin C deficiency to rheumatic fever and rheumatoid arthritis, Experimental, clinical, and general considerations Ann Int. Med 9 586, 1935.

[25] Shank, R. E., Coburn, A F, Moore, L. V, and Hoagland, C F. The level of vitamin A and carotene in the plasma of rheumatic subjects J Clin Investigation 23 289, 1944
[26] Von Glahn, W C, and Pappenheimer, A M Specific lesions of peripheral blood vessels in rheumatism Am J Path 2 235, 1926
[27] Griffith, G C, Phillips, A W, and Asher, C Pneumonitis occurring in rheumatic fever Am. J M Sc 212 22, 1946
[28] Whitelman, W W, and Eckel, J L. The brain in acute rheumatic fever, Non-suppurative meningoencephalitis rheumatism Arch Neurol & Psychiat 28 844, 1932
[29] Bruetsch, W L Late cerebral sequelae of rheumatic fever. Arch Int Med 73 472, 1944
[30] Goldring, W, and Wyckoff, J. Studies of the kidney in acute infection I Observations with the urine sediment count (Addis) in acute rheumatic infection J Clin Investigation 8 569, 1930
[31] Coburn, A F. The Factor of Infection in the Rheumatic State Baltimore, Williams & Wilkins Co, 1931
[32] Sigler, L H Clinical manifestations of rheumatic fever International Clin 3 179, 1933
[33] Swift, H F. Rheumatic fever J A M A 92 2071, 1929
[34] Wilson, M G, and Lubschez, R Recurrence rates in rheumatic fever J A M A 126 477, 1944
[35] Warren, H A, and Choryak, J Cerebral manifestations of acute rheumatic fever. Arch Int Med 79 589, 1947
[36] Coombs, C F. Rheumatic Heart Disease New York, William Wood & Co, 1924
[37] Jones, T D, and Bland, E F Clinical significance of chorea as a manifestation of rheumatic fever J A M A 105 571, 1935.
[38] Ash, R The first ten years of rheumatic infection in childhood Am Heart J 36 89, 1948
[39] Sigler, L H. The Electrocardiogram Its Interpretation and Clinical Application. New York, Grune & Stratton, 1944 Pages 164, 319
[40] Pappenheimer, A M, and Von Glohn, W C Pathology of rheumatic fever Unusual cardiovascular lesions Am J Path 3 583, 1927
[41] Cohn, A. E, and Lingg, C The natural history of rheumatic cardiac disease Modern concepts of cardiovascular disease Am Heart A 11 July, 1942
[42] Bland, E F, and Jones, T D Fatal rheumatic fever Arch Int. Med 61 161, 1938
[43] Juca, A, and White, P D The cause of death in rheumatic heart disease in adults J.A. M A. 125.767, 1944.
[44] Holbrook, W P The army air forces rheumatic fever control program J.A M A 126 84, 1944.
[45] Fullerton, C W The prevention of acute rheumatic fever Canad M. A. J. 52 559, 1945
[46] Wolf, R E, Rauh, L W, and Lyon, R A The prevention of rheumatic recurrences in children by use of sulfathiazole and sulfadiazine J Pediat 27 516, 1945
[47] Kaiser, A D Incidence of rheumatism, chorea, and heart disease in tonsillectomized children J A M A 89 2239, 1927
[48] Roby, W H, and Finland, M Effect of tonsillectomy on acute attack of rheumatic fever. Arch. Int Med 45 645, 1930
[49] Robertson, H F, Schmidt, R E, and Feiring, W The therapeutic value of early physical activity in rheumatic fever Preliminary report Am J M Sc 211 67, 1946
[50] Thomson, A P, and Edgar, S H Effect of variation of diet in rheumatic children Arch. Dis Child 4 152, 1929

[51] Manchester, R. C.: Rheumatic fever in Naval enlisted personnel. Effectiveness of intensive salicylate therapy in cases of acute infection. Arch. Int. Med 78:170, 1946.
[52] Warren, H. A., Higley, C. S., and Coombs, F. S. The effect of salicylates on acute rheumatic fever. Am. Heart J 32:311, 1946.
[53] Wégria, R., and Smull, K. Salicylate therapy in acute rheumatic fever. J. Pediat 26:211, 1945.
[54] Keith, J. D., and Ross, A. Observations on salicylate therapy in rheumatic fever. Canad. M. A. J 52:554, 1945
[55] Harris, T. N. The failure of massive salicylate therapy to suppress the inflammatory reaction in rheumatic fever. Am. J. M. Sc. 213:482, 1947.
[56] Smull, K., Wégria, R., and Leland, J. The effect of sodium bicarbonate on the serum salicylate level. J A M A. 125:1173, 1944
[57] Erganian, J. A., Forbes, G., and Case, D. Salicylate intoxication in the infant and young child. J Pediat 30:129, 1947

CHAPTER XXIII

Bacterial Endocarditis: Acute and Subacute

ENDOCARDITIS and valvulitis of rheumatic origin, described in the previous chapter, cannot be considered a clinical entity It is merely a part of rheumatic pancarditis and of other rheumatic manifestations It assumes significance only insofar as it almost always leaves the affected valve more or less permanently damaged, resulting in cardiac enlargement and ultimately in failure

There are other and rarer forms of endocardial and valvular disease found on postmortem examination and discovered at times during life which are also not specific clinical entities but are parts of generalized debilitating diseases Libman[1] places these into an *indeterminate group* which he divides into two types—an *atypical verrucose* and a *terminal* *The atypical verrucose type* occurs in clinical conditions simulating rheumatic fever but on postmortem examination, no Aschoff bodies are found and the verrucae are larger, flatter and have a tendency to extend over a wider area of the valve and mural endocardium *The terminal type* is occasionally observed as a late manifestation of chronic debilitating disease such as diabetes, gout, nephritis, neoplasms, old lesions of the nervous system, thyroid disease and leukemia The endocardial lesions here consist of small verrucae and there are no characteristic changes in the myocardium and kidneys Libman believes that the lesions are instances of a terminating, not of a terminal disease and are perhaps of infectious or rheumatic origin in spite of the absence of Aschoff bodies

There is a third group of endocarditis which has the characteristics of a distinct disease inasmuch as all the manifestations exhibited by the patient are caused directly by the endocardial involvement This form is known as *bacterial endocarditis* which will be described in this chapter It is true that in an occasional acute case of this disease the primary involvement may exist in another part of the body and the endocarditis is secondary However, even in such cases, the perpetuation of the disease is due to the endocardial process

Bacterial endocarditis has two main diagnostic criteria by which it can be recognized, namely a *bacteriemia* and *embolic phenomena* These differentiate it from the other groups of endocarditis mentioned above Bacterial cultures are on rare occasions obtained also in the other groups but when so obtained are scant Embolic phenomena never occur in the other forms of endocarditis unless mural thrombi, which may serve as emboli, develop in the heart chambers or in the venous system The nature and

origin of these emboli are therefore different from those of bacterial endocarditis where the emboli are derived directly from vegetations due to the endocarditis.

Bacterial endocarditis is divided clinically into an *acute* and a *subacute* form. This is an arbitrary subdivision based mainly on the severity and duration of the disease If the disease is very severe and rapidly progressing, ending in death in less than two months, it is considered acute If more slowly progressing, it is considered subacute. Bacteriologically, likewise, the two forms usually vary. In the acute form, the organisms are usually of the virulent type while in the subacute form, the usual organism is the non-virulent streptococcus viridans. Either type, however, may on rare occasions produce in some cases, the acute and in others, the subacute form as determined by the clinical manifestations

Acute Bacterial Endocarditis

This is by far the rarer form, comprising a small fraction of 1 per cent of all cases of endocarditis. Because of its distructive endocardial changes, it is also known as *ulcerative* endocarditis

Etiology

A variety of organisms have been discovered to produce the disease The more common are the pneumococcus, the streptococcus hemolyticus, the staphylococcus aureus and the gonococcus Those reported less often are the meningococcus, the enterococcus, the influenzal bacillus, the typhoid bacillus, the Brucella malitensis, the tubercle bacillus, the bacillus pyocyaneous and rarely, the streptococcus viridans The last organism produces in the vast majority of the cases the subacute form of the disease.

The focus of infection in acute bacterial endocarditis, unlike that of the subacute form, is in the majority of cases evident. It may consist of a pneumonic process, gonorrheal urethritis, puerperal infection, boils or carbuncles, meningitis, and so on Hussey and co-workers[2] report 4 cases of acute endocarditis occurring in heroin addicts resulting from infections by unsterile needles. In three of these, the tricuspid valves were involved

In most cases, the primary disease antecedes the endocarditis for some time. The invasion of the endocardium by the organism occurs occasionally in a previously damaged area of the endocardium or valve but unlike subacute bacterial endocarditis, this is not the rule. It may involve a normal heart.

Pathology

The disease process usually affects the valve cusps and often also the chordae tendineae, parts of the auricular and ventricular endocardium and in rarer cases, even the intima of the aorta. The area involved be-

comes covered by vegetations of various sizes which are more exuberant and more friable than those of the subacute form. Some of the vegetations may reach the size of a bean. They consist of masses of fibrin, blood cells and extremely large colonies of bacteria Necrotic and suppurative changes occur, often resulting in perforation of the valve leaflets and tear of the chordae tendineae At times, the process invades the myocardium, either by direct extension or by coronary embolization, resulting in multiple abscesses of the heart muscle. It may even extend to the pericardium.

Unlike subacute bacterial endocarditis, where in nearly all cases, the valves of the left heart are involved, in the acute form, we often find involvement also of the valves of the right heart. This is true especially in gonococcal infection

Clinical Manifestations

In those cases where the affection follows directly an acute infectious disease such as pneumonia, puerperal sepsis or meningitis, the condition is usually discovered later in the disease or on postmortem examination Endocarditis should be suspected where the original disease runs an unusually virulent and long course with high temperature, chills, sweat, delirium, coma and marked prostration Repeated examinations of the heart may show progressive changes in its sounds and various murmurs may develop which become more intense and undergo alterations in character as time goes on Various arrhythmias may develop The leukocyte count may reach 30,000 or more and there may be a rapid onset of secondary anemia Embolic phenomena to the brain, kidneys or other organs may be the outstanding manifestations Petechial hemorrhages in the skin and even massive purpuric eruption may occur. The diagnosis will be confirmed by a markedly positive blood culture Although septicemia of the original disease without endocarditis may occasionally yield a positive culture, it is very infrequent and the number of colonies per cubic centimeter of blood is usually scant.

Where endocarditis follows a local infection such as gonorrheal urethritis, skin carbuncles, and so on, it is ushered in by the same train of symptoms and signs described above In any local infection which is followed by symptoms and signs of severe septicemia, we must always suspect the presence of acute endocarditis This is particularly true in cases of gonorrhea which are complicated by joint involvement.

Subacute Bacterial Endocarditis

Subacute bacterial endocarditis usually develops insidiously and progresses more slowly than the acute form. For these reasons, it is also known as endocarditis lenta and chronic ulcerative endocarditis.

Incidence

This form of endocarditis is also comparatively rare, comprising only about 2 per cent of all cardiac disease. It is, however, far more frequent than the acute form It occurs most often between 20 and 40 years of age but no age is exempt. It has been observed in infancy and childhood as well as in senility Rost and Fischer[3] collected 64 cases from the literature, of individuals less than 14 years of age and Zeman[4] reported 18 cases between 60 and 87 years of age In 165 cases reported by Seabury,[5] 2.4 per cent occurred between 1 and 10 years of age, 19.7 per cent between 11 and 20, 64 per cent between 21 and 30, 19 per cent between 31 and 40, 12.1 per cent between 41 and 50; 6.7 per cent between 51 and 60; 4 per cent between 61 and 70 and 1.2 per cent over 70 years. These figures closely approximate those of other similar large series of cases reported by other authors

In the vast majority of cases, the condition develops on a previously diseased valve, most frequently rheumatic or congenital In rare cases, it may affect a valve damaged by arteriosclerosis, syphilis or trauma Roughly, about 25 per cent of cases of chronic rheumatic cardiovalvular disease develop this infection

The disease usually occurs in cases of well compensated valvular disease without auricular fibrillation The absence of auricular fibrillation and decompensation have therefore been used as diagnostic criteria of the disease in doubtful cases Decompensation and auricular fibrillation have also been considered to play some role in the prevention of subacute bacterial endocarditis The author has observed, however, a few cases where subacute bacterial endocarditis coexisted with decompensation or auricular fibrillation Zeman found decompensation in several of his cases and McDonald[6] recently reported an incidence of over 12 per cent of auricular fibrillation in 286 cases of bacterial endocarditis He believes that the comparative infrequency of the coexistence of the two conditions is that cases with auricular fibrillation die before they develop bacterial endocarditis It is very likely that the same reason holds true for cases of decompensation.

The disease occurs with somewhat greater frequency in males than in females. In the series of 328 cases collected from the literature by Blumer,[7] 60 per cent were males and 40 per cent were females In a series of 250 cases reviewed by Kelson and White,[8] there were twice as many males as females.

Etiology

The most common organism producing subacute bacterial endocarditis is the streptococcus viridans which is responsible for the disease in about

90 per cent of cases Recently, certain strains akin to streptococcus viridans have been found in many cases of subacute bacterial endocarditis which have certain distinguishing characteristics Thus, Wheeler and Foley[9] obtained a streptococcus belonging to the Lancefield Group D, often spoken of as the enterococcus group, in 17 out of 21 patients with subacute bacterial endocarditis Loewe and co-workers[10] have isolated a strain of a nonhemolytic streptococcus in 41 cases of subacute bacterial endocarditis which they named streptococcus s b e. having an unusual resistance to penicillin therapy.

In about 5 to 10 per cent of cases, subacute bacterial endocarditis is caused by some of the organisms mentioned under acute bacterial endocarditis Beamer and co-workers[11] report 2 cases where the disease was caused by actinomyces and by histoplasma capsulatum They reviewed 10 other previously reported cases from the literature caused by higher bacteria, yeasts or fungi Hitzig and Liebesman[12] report a case caused by spirillum minus

Unlike acute bacterial endocarditis where the process usually accompanies a known disease, the subacute form, in the majority of cases, develops apparently spontaneously It may, in some cases, follow an upper respiratory infection, the extraction of a tooth or other surgical procedures In such cases, we assume that the invasion of the blood stream by the bacteria occurred at the sites of the original infection in sufficiently large amounts to overcome the defensive mechanisms of the patient. This, however, is not the rule In most cases, it develops insidiously, without any demonstrable focus of infection It may follow prolonged strain, exposure to inclement weather, insufficient rest, improper nutrition or other factors that lower the resistance of the individual The lowered resistance evidently prevents the destruction of the low virulent streptococcus viridans which is a frequent invader of the blood stream but which normally is easily destroyed by our protective defenses

Pathology

As indicated before, in the vast majority of cases, the infection settles and propagates in a valve which was previously damaged by rheumatic or other disease or which is congenitally defective, such as a bicuspid aortic valve It has also been observed in the form of *endarteritis* at the site of a patent ductus arteriosus or in an arterio-venous aneurysm Lipton and Miller,[13] reported a case of the latter condition occurring in the left thigh which was cured by operation and they cite two other cases from the literature

The characteristic lesion consists of vegetations which are much larger and are more easily detachable than those of rheumatic fever They are

smaller, however, than those of acute bacterial endocarditis and are proliferative rather than destructive. Their color is pinkish, yellowish or greenish and they become grayish as they grow older. They are less friable than the lesions of acute bacterial endocarditis. As the involvement progresses, it undergoes fibrosis, especially at the base and calcific infiltration may take place.

The lesions have a tendency to extend from the valves to the mural endocardium. Thus, in mitral valve involvement, the process often extends



FIG 112.—VEGETATIONS, V, OF SUBACUTE BACTERIAL ENDOCARDITIS. They are superimposed on the aortic valve and extend to a congenital interventricular septal defect, indicated by white probe, P, in the membranous portion of the interventricular septum. The exposure shows the interior of the left ventricle. (From Edwards, Postgraduate Medicine 3 329, 1948. Courtesy of the author and publishers.)

to the left auricular endocardium and to the chordae tendineae. In aortic involvement, it may extend to the left ventricular endocardium, as shown in Figure 112.

masses are lodged on the surface of the valves, uncovered by endothelium. The deeper parts of the lesions show fibroblastic proliferation, which extends to the valve itself. The substance of the valve undergoes inflam-

matory changes like that of rheumatic fever, with many scattered mononuclear cells.

According to Allen,[14] the vegetations are made up of three zones. The *inner zone*, which comprises the bulk of the lesions, consists of a mass of fibrin and blood cells with various degrees of necrosis. The *middle zone* consists of bacteria. The *outer zone*, which is a fraction of a millimeter thick, consists of a layer of fibrin derived from the blood stream. The vegetations grow by the propagation of the inner zone and emboli are probably fragments broken off from the inner zone.

The myocardium shows very little change in most cases. There may be fatty degeneration and cloudy swelling of the muscle and occasional areas of infiltration of mononuclear cells in the interstitial tissue. Clawson and Bell[15] have demonstrated Aschoff bodies in 11 per cent of their cases and in others, the so-called Bracht-Wächter bodies. The latter are small lesions in the myocardium, composed of necrotic areas with polymorphonuclear leukocytes and a serous exudate.

The pericardium is rarely involved by the inflammatory process. Small hemorrhages may be observed.

Pathogenesis

The mechanism of the production and localization of the lesion has been the subject of considerable investigation. Libman believed that the greater stress and strain thrown on the valves of the left heart is responsible for the usual location of the disease in those valves, especially the mitral. Friedman and co-workers[16] produced the lesions by inserting capsules containing infected blood agar into the ventricle. Vegetations developed only on those valves that came in contact with the capsules In the early stage, proliferative changes occurred and later, fibrin deposited and made up most of the lesions. They believe that the development of the lesion is caused by the deposit of fibrin and platelets which prevents the bactericidal agents of the blood from acting locally on the microorganism. In addition, the fibrin offers an excellent culture medium for the growth of bacteria. Allen believes that inasmuch as in the majority of cases subacute bacterial endocarditis is superimposed on rheumatic endocarditis, the latter lesion plays a part in the pathogenesis of the vegetations of bacterial endocarditis. The fibroblastic deformity of the rheumatic lesion takes the form of a projecting shelf or barrier, usually in the line of closure, against which the blood stream strikes. The site of this deformity suffers a greater impact during systolic discharge than a normal valve because it does not yield as easily as a normal valve. There is thus greater contact of the diseased valve with the blood carrying the bacteria and therefore easy infection. This is enhanced by the diastolic backflow due to insufficiency that often coexists. The same mechanism applies to congenital lesions.

There is a possibility that in some cases, the lesion is produced not by implantation of the infection on the surface of the valve but by its invasion of the valve through its capillary supply. It has been established by Gross and other workers that the vascularity of the valves is greatly increased as a result of rheumatic disease.

Clinical Manifestations

In the majority of cases, the onset of the disease is insidious At first, the patient finds that he gets easily fatigued, especially towards the afternoon and as time goes on, the sense of fatigue becomes more marked and more prolonged so that he is unable to persue his accustomed work. He develops marked lassitude and he may experience a feverish feeling with or without chills or sweat These are more apt to occur late in the afternoon or evening A temperature determination may show a rise to 101 degrees F If the temperature is followed daily it may be found to vary greatly It is usually of the remittent type, being within normal range for one or more days followed by a variable rise on other days In later stages or where embolic phenomena dominate the picture, it may rise to as high as 103 degrees or even 106 degrees F. and may assume an intermittent form

As the disease advances, there is a gradual onset of pallor which becomes progressively more marked and assumes the characteristic café au lait appearance. Anorexia, loss of weight and localized pain in various parts of the body may develop

During the course of the disease, several important signs may appear which are more or less pathognomonic, although they occur in other diseased states. Of these, the most important are petechiae, Osler's nodes, a palpable spleen, clubbing of the fingers, retinitis and embolic phenomena

The incidence of occurrence of these manifestations varies in the different reported series of cases This variation may perhaps be accounted for by differences in the length of time the individual case has been under the care of a given observer Most of the manifestations are either fleeting or develop late in the disease and may therefore be overlooked by one or another observer who watches the case a comparatively short time.

Petechiae: These occur very frequently in this disease Libman and Friedberg[11] observed them in 80 per cent of their cases They are very minute red spots, measuring over 2 millimeters in diameter and do not disappear on pressure They usually appear in crops and are more frequent about the hands, feet and in the mucous membranes of the conjunctivae and mouth. They may, however, occur in any other part of the body. If they occur under a nail, they assume a linear shape, spoken of as "splinter hemorrhage." Each petechia usually fades within a few days.

Petechiae have been supposed to be due to emboli but the accepted explanation is that they are caused by toxic capillary damage and diapedesis of red cells into the skin. They occur in a great many other conditions than in subacute bacterial endocarditis There is a possibility, however, that some spots resembling petechiae but having a whitish center are embolic

Osler's Nodes.[11] These occur in about 25 to 50 per cent of cases of subacute bacterial endocarditis at one time or another. They are painful, tender, purplish, indurated nodules which may reach the size of a pea or larger, appearing suddenly and usually disappearing very slowly over a period of a few days They are found most frequently about the fingers and toes, usually the volar surfaces, as well as on the thenar and hypothenar eminences. They are also observed over the lower parts of the arms They are embolic or hemorrhagic in origin In some cases, the pain produced by these nodes may first bring the patient to the doctor The author observed a man, 45 years of age, who came with complaints of pain in his feet on walking Inspection of the soles of his feet revealed many of these nodes Examination showed some elevation in temperature and pulse rate, a harsh systolic apical murmur and moderate enlargement of the spleen His future course was characteristic of subacute bacterial endocarditis and repeated blood cultures yielded streptococcus viridans.

Enlargement of the Spleen This is observed in about 65 per cent of cases. Libman and Friedberg detected it in 80 to 90 per cent of their cases. In some, the enlargement may be very marked and in rare cases, it may extend almost as far as the umbilicus In most cases, however, it is slight and in some of these it may, at times, be difficult to decide if enlargement is actually present The organ, when felt, is smooth and firm, but not tender The enlargement is due to toxemia, not to embolization. Splenic enlargement due to embolization is usually associated with marked pain, and tenderness due to perisplenitis

Clubbing of the Fingers: This occurs in marked forms in about 20 per cent of cases Milder grades of clubbing may be observed more frequently, perhaps in as many as 60 per cent of cases. It usually develops late in the disease In a certain proportion of cases, the toes, likewise, show clubbing

The pathogenesis of clubbing in this disease is not quite understood. It is probably due to the toxemia, producing dilatation of the arteriolo-venular junctions in these regions which results in a greater blood accumulation and growth of the soft tissues. We must always rule out congenital or occupational clubbing in evaluating this diagnostic sign in subacute bacterial endocarditis

Retinitis: This may develop in about 20 per cent of cases. It usually consists of flame shaped hemorrhagic spots as seen in other diseased states such as in the severe anemias, leukemias and vascular disease or hypertension. Doherty and Trubek[19] described a characteristic "canoe shaped" linear hemorrhagic spot with a light central area which they consider pathognomonic of bacterial endocarditis It appears suddenly and vanishes without leaving any trace The only other condition in which they found this lesion was severe pernicious anemia.

Embolic Phenomena These are by far the most important manifestations of subacute bacterial endocarditis They are of great help in the diagnosis of the disease, although they often mislead us in diagnosis, especially in the early phases before their nature and origin can be determined.

In Seabury's series, 6 7 per cent of cases showed an acute embolic onset without any previous illness In 57.7 per cent, embolic phenomena occurred in the course of the disease. It is very likely that the incidence of embolization is much greater. There is a probability that it may occur in every case at one time or another It is not always detected because it often strikes areas of the body which may yield insufficient symptoms or signs by which it can be recognized

The outstanding symptoms and signs of embolization depend upon the area of the body involved Thus, *embolization to the brain or other parts of the central nervous system* may yield a train of neurologic disturbances similar to those seen in local inflammation, neoplasm, vascular hemorrhage or thrombosis If, as occasionally happens, such embolization occurs as an early manifestation of the disease, the case may go to a neurologist or neurosurgeon before the true underlying condition is discovered. The author has observed several such cases In one instance operation for a brain abscess was contemplated before the true nature of the disease was ascertained In another case, a spinal tumor was suspected early in the disease

Embolization to the kidneys will produce hematuria and pain which may, at times, be mistaken for renal colic. The occurrence of albumin and pus cells in the urine together with the elevated temperature and tenderness in the kidney regions may also lead to a mistaken diagnosis of pyelonephritis

Embolization to the spleen resulting in perisplenitis may produce left upper abdominal pain, tenderness and rigidity which may be mistaken for an acute surgical upper abdominal condition. This pain, appearing as it often does mainly on respiration, may also be mistaken for an acute pleuropneumonic process. Embolization to other intra-abdominal arteries may produce symptoms and signs of an acute surgical abdominal condition. Embolization to a main artery of an extremity may result in gangrene.

Cardiac Manifestations: As indicated before, in the vast majority of cases, subacute bacterial endocarditis develops on a pre-existing valvular disease or congenital defect. The outstanding cardiac findings, therefore, are those caused by such pathologic states. The characteristic murmur or murmurs of the underlying valvular defects are always found, except in rare cases of mural endocarditis. In Kalson and White's series of 250 cases, only 2 cases showed no murmurs.

If a case of subacute bacterial endocarditis is observed over a long period of time, it will be found that the pre-existing murmur undergoes progressive changes in its character, intensity and in the extent of its transmission. The kind of murmur previously present which undergoes such changes helps us to determine which valve is affected. Thus, if a systolic murmur of pre-existing mitral insufficiency shows progressive changes, the pathologic process is located in the mitral valve. If a diastolic murmur of aortic insufficiency undergoes progressive changes, the pathologic process involves the aortic valve. If both valves showed pre-existing disease, the valve which exhibits progressive changes in the pre-existing murmur is the one which has the bacterial invasion. The discussion of murmurs by which valvular disease or congenital defects are recognized is found in Chapters XXII and XXVII

It must be remembered that a systolic murmur may occur in prolonged infections and in anemic and febrile states even if there is no valvular disease, as discussed in Chapter IX Hence, if no other evidence of valvular disease is present, the diagnosis of subacute bacterial endocarditis is to be seriously questioned, unless substantiated by repeated positive cultures.

The author is reminded of a male patient, 30 years old, seen many years ago, who was running an intermittent temperature with occasional chill and sweat for about four months There was a gradual onset of anemia, gastro-intestinal disturbances, progressive weakness, some enlargement of the spleen and slight pain in the right lower quadrant of the abdomen As time went on, some liver enlargement was noted, and a low intensity systolic murmur developed over the left precordium, not localized to any particular valve area. Although blood cultures were negative on several occasions, the diagnosis of mural subacute bacterial endocarditis with mesenteric embolization was entertained by several competent clinicians

[illegible]

nosis of subacute bacterial endocarditis in the absence of definitely demonstrable valvular disease or congenital defect.

Besides the characteristic murmurs of pre-existing heart disease which undergo changes in the course of superimposed bacterial involv

are no other specific cardiac findings that are pathognomonic of the disease. Some arrhythmias, especially ectopic contractions may develop but they are not characteristic. As the valvular damage progresses, heart failure may supervene with its characteristic train of symptoms and signs. This is seen more often now since the use of penicillin. Previously, most patients were carried off by the disease before failure developed

Laboratory Aids in Diagnosis

The most important diagnostic criterion of subacute bacterial endocarditis is a positive blood culture This is usually obtained in blood drawn from a vein. According to Mallén, Hube and Brenes,[20] the highest incidence of positive cultures occurs in blood drawn from bone marrow. They found, however, no definite superiority of blood obtained for culture from sternal bone marrow over that of the radial artery or antecubital vein in 88 patients with subacute bacterial endocarditis. The easier and safer way of obtaining venous blood for culture is therefore preferable.

To obtain a proper blood culture, it is essential to avoid contamination while collecting the blood The most frequent contaminants are staphylococcus albus, diphtheroid bacilli and B subtilis, but occasionally, nonhemolytic streptococci may also be contaminants It is essential that blood be drawn at the time when the fever is highest and when no sulfa drugs or penicillin have been used

Positive cultures are most frequently obtained in fluid media If a quantitative determination is desired after a positive culture has been obtained, plating of 1 or 2 c c. of blood on agar may then be done and the number of colonies counted In many confirmed cases, plating may yield negative results while fluid media will be positive. The fluid media most often used are hormone broth and 0.2 per cent glucose with an optimum pH of 7 4 to 7 6 , but other media are also employed in specific cases

It is essential that no blood culture be considered sterile until it has been in incubation for at least ten days. In rare cases, a positive culture may be obtained even later It is advisable, therefore, not to discard the culture before twenty days. Usually, however, growth occurs before the seventh day.

Many cases of subacute bacterial endocarditis may yield a negative culture on one or more occasions and be positive on others. It is therefore essential that repeated cultures be taken before the diagnosis is eliminated It is also essential that positive cultures be obtained on at least two occasions to make a definite diagnosis of the disease. One scantily positive culture obtained after repeated trials is no proof of the presence of the disease unless the clinical course is characteristic. An occasional weak culture of streptococcus viridans has been obtained in rheumatic fever, in rheumatoid arthritis and other conditions by various observers.

The blood count in subacute bacterial endocarditis varies in different cases. In many cases, the white cell count is within normal limits throughout the course of the disease and in rare cases, there may even be a moderate or marked leukopenia. In about one-third of all cases, there is a mild leukocytosis, the count varying between 10,000 and 15,000 white cells per cubic millimeter and in about 15 per cent of cases, it may vary between 15,000 and 20,000 or even higher. In all cases, there is some fluctuation in the white cell count with changes in temperature and with the appearance of embolization.

The red cell count varies with the duration and severity of the disease as well as with the presence or absence of congestive failure. Early in the disease, the count may be normal and may remain within normal range several months. In most cases, the red cell count gradually diminishes to as low as 2,500,000 cells per cubic millimeter of blood and in about 10 per cent of cases, it may come down to much lower figures, even to less than 1,000,000, if untreated. The hemoglobin drops correspondingly, the color index remaining less than 1 in most cases. In the presence of congestive failure, capillary stasis may result in a high red cell count and thus give a false impression of the actual hemic condition.

The urine, as said before, may contain many red blood cells which indicates in some cases, renal infarction, in others, glomerular lesions and in still others, perhaps capillary rhexis. Albuminuria is a frequent finding.

Differential Diagnosis

There is a great variety of acute and subacute febrile diseases which may be mistaken for subacute bacterial endocarditis and vice versa The most frequent are rheumatic fever, typhoid fever, tuberculosis, splenic anemia, pyelonephritis, pylophlebitis, deep seated abscesses, undulant fever, various septicemias and acute surgical abdominal conditions where the onset of signs of endocarditis is heralded by mesenteric embolization Of these, the most important conditions that require urgent differential diagnosis are cases of subacute bacterial endocarditis simulating acute surgical conditions and conditions requiring surgical interference which simulate subacute bacterial endocarditis The former may often undergo unnecessary surgery which further endangers the life of the patient. The latter requires surgical interference to save the life of the patient, as exemplified by the following case:

A girl, 11 years old, developed a persistent intermittent temperature of several months duration, marked weakness, secondary anemia, occasional pain in the right upper abdomen and a systolic murmur over the left precordium, not localized to any particular valve area. Although repeated blood cultures were negative, the attending physicians considered the case one of subacute bacterial endocarditis. This being in the

iod, a hopeless prognosis was given. Careful physical examination left no doubt in the author's mind, however, that the child suffered from a right subphrenic abscess This was confirmed by x-ray which showed marked elevation of the right dome of the diaphragm. Surgical interference resulted in complete recovery

The differentiation of subacute bacterial endocarditis from the medical conditions mentioned above is usually easy if the patient is carefully examined and repeated laboratory studies are made. Some points in the differential diagnosis of typhoid fever, rheumatic fever and undulent fever have been mentioned in the previous chapter. Pulmonary tuberculosis may be detected by careful physical and roentgenologic examinations of the lungs and repeated sputa examinations. Splenic anemia or so called Banti's disease may be confused with subacute bacterial endocarditis only *in the early stages In the cirrhotic stage with recurring ascites, the diagnosis is distinctive*

In our differential diagnosis, two facts must always be borne in mind to rule out subacute bacterial endocarditis One is the absence of definitely demonstrable pre-existing valvular and congenital heart disease The other is a repeatedly negative blood culture. Although the disease may perhaps develop in rare occasions in previously healthy hearts, it is extremely uncommon. Likewise, although the septicemias, pylophlebitis and deep seated suppurative infections may yield occasionally a positive blood culture, the organism is usually not streptococcus viridans. Repeated positive cultures of this organism may be taken as corroborative evidence of the disease and repeated negative cultures would tend to rule out the disease

Prognosis

Both acute and subacute bacterial endocarditis have almost always been fatal diseases up to the advent of penicillin therapy. Libman and Friedberg[17] estimated that the incidence of sponaneous recovery in subacute bacterial endocarditis was 3 to 5 per cent. In a review of the literature by Lichtman[21] up to 1943, covering 704 cases treated with sulfa drugs, the total average incidence of recovery was 5.5 per cent which corresponds fairly closely to the spontaneous recovery rate of Libman and Friedberg

The author's belief is that some of the so-called cured cases of subacute bacterial endocarditis in the past probably did not suffer from the disease. This is true, especially, where a scantily positive blood culture was obtained with difficulty after many trials As said before, a scantily positive culture does not always prove that the disease existed even in the presence of valvular disease In 72 definitely proved cases of subacute bacterial endocarditis, seen before the advent of penicillin therapy, the author cannot recall a single recovery.

Since penicillin came into use, the prognosis in this disease has markedly altered. This is one specific example of the life saving effect of the drug. At the present writing, about 75 per cent of definitely proved cases of subacute bacterial endocarditis recover from the disease by the use of this product. Many other cases have shown temporary improvement. The incidence of acute bacterial endocarditis has also greatly lessened because of the early use of this antibiotic. We must still wait, however, to find out how long the recovery will last in many of the cases. It must be remembered that the pre-existing structural endocardial disease which predisposes to the infection, remains and becomes aggravated by the bacterial involvement. Further reinfection may, therefore, take place at a later period. We must also realize that the average span of life of these cases is shorter than of normal individuals and sooner or later they die as a result of decompensation, embolization from mural thrombi in the chambers of the heart, or other conditions. If we can prolong their lives, however, to their approximately natural span and make them useful, we accomplish much.

Penicillin Therapy

The beneficial effects of penicillin in subacute bacterial endocarditis was first reported by Loewe and co-workers[22] and by Dawson and Hobby[23] in 1944. The former authors have attributed their success partly to the addition of heparin to the penicillin therapy. It has since been shown, however, that heparin is not necessary for a successful outcome. In fact, several authors have demonstrated that heparin may have harmful effects in this disease. According to Levy and McKrill,[24] it favors fragmentation of the vegetations, predisposing to embolization, and it also favors the production of hemorrhage. One of their cases died from a large cerebral hemorrhage, as shown at autopsy.

Mode of Action: The successful destructive effect of penicillin on the infected organism in this disease is probably due to its power of penetration into the vegetations, as was shown by Nathanson and Liebhold.[25] It thus is able to destroy the deep seated colonies which are beyond reach of other germicides, including the sulfa drugs. To bring about a complete cure, however, considerable time is necessary for absorption and organization of the vegetations. It is possible that some microorganisms remain buried in the fully organized granulation tissue which can not be penetrated by the penicillin. This would account for recurrences of the infection if treatment is not thorough, and long enough. In an apparently cured case where the disease ended in death due to heart failure, Bloomfield and Halpern[26] found a few cocci in the flat scars of previous vegetations.

Dosage: The dosage of penicillin required in the successful therapy of any case depends upon the sensitivity of the causative microorganism.

This may be determined by testing the microorganisms obtained from blood cultures for in vitro sensitivity to penicillin by the serial dilution method The more resistant the organism, the greater the dosage required An effort should be made to maintain a penicillin level of about ten times the in vitro sensitivity figure.

The most reliable test, however, is the clinical result obtained from a given dosage It is, perhaps, safest to start with a daily dosage of not less than 600,000 units, although earlier, we[27] had reported good results in some cases with a daily dosage of 300,000 units If the response is not satisfactory in several days, the dosage should be tripled In some cases, we may have to use as much as 4,000,000 units per day and even more

Routes of Administration The continuous intravenous drip is perhaps the best method of maintaining a constant blood penicillin concentration It is, however, inconvenient and not always practical For these reasons, the interrupted intramuscular injections may often be employed to better advantage The daily dose is divided into twelve portions, and given at two hour intervals It is essential, however, that the injections are not spaced at longer intervals, for the blood penicillin level drops fast, one hour after the injection, and the level is very low at the end of two hours

Priest and co-workers[28] recommend a minimal dose of 100,000 units to be given at ninety minute intervals if the intramuscular route is used. However, many cases respond well to 50,000 units at two hour intervals, and this should be tried first If the response is not satisfactory, the larger doses may be used at more frequent intervals Restriction of fluid intake to no more than 1,000 cc during the day may reduce the fluctuation of the serum penicillin level

Beyer and co-workers[29] advise the use of continuous intravenous infusion of penicillin in a 6 per cent sodium para-amino-hyspurate solution This drug raises the blood concentration of penicillin by reducing its elimination through the kidneys. This method, however, is best used in very obstinate cases

The newer preparations of penicillin dissolved in beeswax and oil according to the Romansky and Rittman[30] formula and the other similar preparations being placed on the market recently, which are said to maintain a good penicillin level by injecting 300,000 units or more in one daily dose, may in the future prove to be of value In this disease, however, it is not as yet safe to rely on these preparations until definite proof is forthcoming of their complete effectiveness.

Duration of Treatment: This depends upon the virulence of the organism and its resistance to therapy as well as the duration of the disease, when treatment is first started. If treatment is started very early in the disease, and the organism is penicillin sensitive, recovery may follow in four weeks. If seen late, or if the organism shows considerable resistance to penicillin,

treatment may have to be continued for eight weeks, and in some cases much longer. Some unusually obstinate cases may require several months of continuous therapy to effect a cure In the latter cases it is essential to increase the amount of penicillin continually. Therapy should not be discontinued in any case until we are definitely sure that a cure is complete

The criteria of complete recovery are a continuously normal temperature and pulse rate for three or more weeks, a normal blood count including the leukocytes, red cells and hemoglobin, repeatedly normal blood cultures on four or more consecutive trials and a decided improvement of the general condition of the patient The last includes a gain in weight, improvement in color and the absence of symptoms and signs of embolization or other evidence of the disease.

When all findings indicate complete cure, it is essential to observe the patient daily for three or four more weeks and at weekly intervals for several months after he is discharged from direct supervision During this period, the patient is to report on the recurrence of any symptoms or on any rise in temperature Repeated blood cultures at monthly intervals are also advisable.

Other Therapeutic Measures

In very obstinate cases, the author has used streptomycin in doses of one to two grams daily, given intramuscularly in addition to penicillin, with good results Its value in cases of penicillin resistant organisms was demonstrated by Priest and McGee.[31]

In cases who present a marked secondary anemia, several blood transfusions will expedite recovery A high caloric diet with the addition of large amounts of the vitamins and iron preparations is essential

Bed rest should be continued until the temperature and pulse return to normal and remain so at least one week. The patient may then be gradually allowed out of bed while the treatment is continued.

If congestive failure develops during the treatment or after recovery from subacute bacterial endocarditis its treatment should be carried out as discussed in ChapterXIII

Therapeutic Failures

About 15 to 25 per cent of cases fail to respond to the various therapeutic measures employed, and eventually succumb to the disease. Failures occur most frequently in those cases that come under observation late in the disease In some cases, failure may be due to inadequate dosage of penicillin In others, allergic reaction to the antibiotic may be a cause, as shown by Hines and Kessler[32]

Some cases are apparently cured of the infection but death may result from embolic glomerulonephritis, or from rupture of a mycotic aneurysm,

cerebral or pulmonary embolization or congestive failure. The last named condition may occur many months after the patient has been symptom free of subacute bacterial endocarditis, and is mainly due to the valvular damage caused by the disease.

REFERENCES

[1] Libman, E Characterization of various forms of endocarditis J A M A 80 813, 1923.
[2] Hussey, H H, Kelliher, T F, Schaefer, B F, and Walsh, B J Septicemia and bacterial endocarditis resulting from heroin addiction J A M A 126 535, 1944
[3] Rost, W L, and Fischer, A E Subacute bacterial endocarditis in childhood Report of 12 cases Am J Dis Child 36 1144, 1928
[4] Zeman, F D Subacute bacterial endocarditis in the aged Am Heart J. 29 661, 1945
[5] Seabury, J H Subacute bacterial endocarditis Arch Int Med 79 1, 1947
[6] McDonald, R K The coincidence of auricular fibrillation and bacterial endocarditis Am Heart J 31 308, 1946
[7] Blumer, G Subacute bacterial endocarditis Medicine 2 105, 1926
[8] Kelson, S R, and White, P D Notes on 250 cases of subacute bacterial endocarditis studied and treated between 1927 and 1939 Arch Int Med. 22 40, 1945
[9] Wheeler, S M, and Foley, G E A note on the serologic classification of streptococci isolated from subacute bacterial endocarditis Am Heart J 30 511, 1945
[10] Loewe, L, Plummer, N, Niven, C F, Jr, and Sherman, J M Streptococcus s b e in subacute bacterial endocarditis J A M A 130 257, 1946
[11] Beamer, P R, Reinhard, E H, and Goodof, I I Vegetative endocarditis caused by higher bacteria and fungi Am Heart J 29 99, 1945
[12] Hitzig, W M, and Liebesman, A Subacute endocarditis associated with infection with a spirilum Arch Int Med 73 415, 1944
[13] Lipton, S, and Miller, H Streptococcus viridens septicemia subacute bacterial endocarditis of an arterio-venous aneurysm J A M A 126 766, 1944
[14] Allen, A C Mechanism of localization of vegetations of bacterial endocarditis Arch Path 27 399, 1939
[15] Clawson, B J, and Bell, E T A comparison of acute rheumatic and subacute bacterial endocarditis Arch Int Med 37 66, 1926
[16] Friedman, M, Katz, L N, and Howell, K Experimental endocarditis due to streptococcus viridans Arch Int Med 61 95, 1938
[17] Libman, E, and Friedberg, C K Subacute Bacterial Endocarditis New York, Oxford University Press, 1941
[18] Osler, W Chronic infectious endocarditis Quart J Med 2 219, 1909
[19] Doherty, W B, and Trubek, M Significant hemorrhagic retinal lesions in bacterial endocarditis (Roth's spots) J A M A 97 308, 1931
[20] Mallén, M S, Hube, E L., and Brenes, M Comparative studies of blood cultures made from artery, vein and bone marrow in patients with subacute bacterial endocarditis Am. Heart J 33 692, 1947
[21] Lichtman, S S Treatment of subacute bacterial endocarditis Current results Ann Int. Med 19 787, 1943
[22] Loewe, L., Rosenblatt, P, Greene, H J, and Russel, M. Combined penicillin and heparin therapy of subacute bacterial endocarditis J.A M A 124 144, 1944
[23] Dawson, M. H, and Hobby, G L. The clinical use of penicillin—Observations in 100 cases. J.A M.A. 124 611, 1944
[24] Levy, L, and McKrill, N.: Results in the treatment of subacute bacterial endocarditis. Arch Int Med. 77 367, 1946

[25] Nathanson, M H, and Liebhold, R A. Proc Soc. Exper Biol & Med. 62 83, 1946
[26] Bloomfield, A L, and Halpern, R M The penicillin treatment of subacute bacterial endocarditis J A M A 129 1135, 1945
[27] Sigler, L H, Longo, T J, and Feldman, H H Treatment of subacute bacterial endocarditis with penicillin—Report of ten cases New York State J Med 46 624, 1946
[28] Priest, W S, Smith, J M, and McGee, C J Penicillin therapy of subacute bacterial endocarditis Arch Int Med 79 333, 1947
[29] Beyer, K H, Flippin, H, Verwey, W F, and Woodward, R The effect of para-aminohippuric acid on plasma concentration of penicillin in man J A M A 126 1007, 1944
[30] Romanski, M J, and Rittman, G E Prolonging the action of penicillin Science 100 196, 1944
[31] Priest, W S, and McGee, C J Streptomycin in the treatment of subacute bacterial endocarditis J A M A 132 124, 1946
[32] Hines, L E, and Kessler, D L *Ineffectiveness of penicillin in some cases of bacterial endocarditis* Quart Bull Northwestern Univ Med School 19:296, 1945

CHAPTER XXIV
Chronic Cardiovalvular Disease

Introduction

From a pathologic viewpoint, chronic cardiovalvular disease is the end product of inflammation, degeneration, trauma or congenital defects of a given valve If the pathologic changes of the valve interfere with the normal cardiac propulsion or expulsion of blood, they will be accompanied by certain clinical manifestations If they do not offer any interference, they may be overlooked during life and discovered only at autopsy Contrariwise, signs of valvular defects may occur during life in the absence of structural disease of a valve where it is caused by functional inadequacy of the given valve We often find a normal valve at autopsy where a diagnosis of disease of that valve was made during life It will thus be seen that whether a valve is deficient structurally or functionally, its interference with normal circulatory dynamics during life is the factor which determines the diagnosis

We shall attempt to present here the various forms of chronic valvular disease, their clinical manifestations and recognition

Etiology

Of the inflammatory processes that may produce chronic valvular disease, rheumatic fever is the most frequent Next in frequency is syphilis and least, subacute bacterial endocarditis These have been fully described in previous chapters Whether or not other infections may produce chronic valvular disease has not been definitely established

Of the degenerative processes, arteriosclerosis is the underlying cause

Congenital valvular deformities are rare and are discussed in Chapter XXVII Traumatic rupture of a valve is also comparatively rare It may occur as a result of sudden severe compression of the chest, sudden severe blow to the chest or sudden strain

Thus, the most frequent etiologic factor of valvular disease in early life is rheumatic fever Most individuals with rheumatic heart disease have died before 45 years of age, and the degenerative group of valvular disease begins to have its ascendency in those above this age. The syphilitic group usually appears after 30 years of age and continues on through the degenerative age, comprising at all times, only a very small percentage of cases.

In the rheumatic group, the most frequent valves affected are the mitral and aortic, the former being about three times as frequent as the latter. In a certain proportion of cases, both are involved In an occasional case,

the tricuspid and the pulmonic valves may be involved. In syphilis, only the aortic valve may be involved and if mitral pathology is also present, we must always consider an additional etiologic cause such as the rheumatic, arteriosclerotic or other In arteriosclerosis, the mitral or aortic valve or both may be affected

Subacute bacterial endocarditis was a rare cause of chronic valvular disease until recent years, because the infection carried off the sufferer in the vast majority of cases before chronic crippling of the affected valve occurred. With the advent of the successful penicillin therapy in the disease, the incidence of chronic valvular disease due to this cause will undoubtedly greatly increase in years to come. It must be remembered, however, that inasmuch as the disease usually develops on a previously damaged heart due to other disease, this etiologic factor may, in most cases, merely be an additional cause of the given chronic valvular disease

The reason for the much greater incidence of valvular disease in the left heart than in the right is probably the greater strain and stress to which the left heart valves are exposed during the process of opening and closing under high tension Fatigue and traumatization of these valves probably lower their resistance and predispose them to more frequent infection and degeneration

Clinical Manifestations

The clinical manifestations of valvular disease depend upon the extent of valvular damage and upon the valve which is affected

Symptoms In the majority of cases, especially where the valvular damage is not marked, the condition is asymptomatic under ordinary circumstances Under moderate physical or mental strain, not enough to affect a normal individual, however, some dyspnea may occur. In occasional cases, the anginal syndrome may manifest itself under such circumstances, especially in aortic valvular disease In aortic stenosis, if extensive, syncope is occasionally observed and even sudden death may occur as was shown by Marvin and Sullivan [1] As time goes on, congestive failure may ensue in all valvular disease when symptoms referable to such failure will develop

Signs The outstanding sign of chronic valvular disease is the *murmur* which has certain features characteristic of the given valvular disease. In mild cases, this may be the only sign and it is therefore difficult at times to determine if the murmur is due to valvular disease or is of nonorganic origin In more advanced cases, however, there may be some changes in the character of the heart sounds and enlargement of one or more of the chambers of the heart corresponding to the given valvular disease. In some forms of valvular disease, there are also certain characteristic peripheral vascular signs which help in the diagnosis All these will be described under the individual valvular disease

Disease of the Mitral Valve

Pathology

The chronic pathologic changes that may affect the mitral valve may vary from slight thickening of the cusps, unrecognized clinically, to a severe grade of deformity. The latter may consist of a fusion of the cusps and narrowing of the osteum in various degrees. In some long standing and advanced cases, calcific infiltration may occur. The orifice may become extremely narrow and rigid and assume different shapes, variously spoken of as "buttonhole," "fish mouth" and so on. Cases of this kind



Fig 113—Section of the Mitral Valve at its Attachment Marked fibrosis of its entire thickness with some calcification close to the auricular surface. The latter shows some destruction and denudation of the surface endothelium From a case of old rheumatic mitral stenosis and recurring rheumatic carditis. × 57

produce the clinical picture of mitral stenosis with or without regurgitation depending upon the condition of the mitral leaflets and the chordae tendineae.

In some cases, the fusion of the valve is not marked and the main involvement is of the chordae tendineae, resulting in their shortening and retraction. The valve leaflets are thus pulled downwards and apart, producing the predominant clinical effect of mitral insufficiency. The same effect may also be produced where the mitral leaflets or chordae tendineae are torn, which is more apt to occur in traumatic injuries, although it may occur also as a result of disease.

Miscroscopic examination reveals marked fibrosis and some calcific infiltration, as shown in Figure 113.

In old age, sclerotic changes and calcific infiltration may occur in the mitral as well as in the aortic ring, with or without involvement of the leaflets. This condition is spoken of as "annular sclerosis." If the leaflets are not markedly involved, there is usually no interference with the function of the given valve.

In functional insufficiency of the mitral valve, there may be no structural damage of the valve leaflets or of the chordae tendineae. It may occur in conditions of left ventricular dilatation. The mitral insufficiency here may be due either to an associated dilatation of the auriculo-ventricular ring, or to the pulling downward of the chordae tendineae by the dilated left ventricular wall, or to both.

We also see cases where a murmur like that of mitral stenosis is heard during life, and no evidence of such stenosis is found at autopsy. Thus, in an autopsy study of 68 cases where such a murmur was heard during life, Bland and co-workers[2] found that only 24 had stenosis. In 19 others, there was merely wrinkling and deformity of the mitral leaflets, but no stenosis. In the remaining 25 cases, there was only minimal thickening of the free margins of the mitral leaflets. The explanation of the murmur in such cases may vary. In some, marked left ventricular dilatation due to aortic insufficiency or other causes without concomitant dilatation of the auriculo-ventricular ring, produces a mechanical effect similar to that of mitral stenosis. The condition is often spoken of as relative mitral stenosis. This may also partly explain the Austin Flint murmur. Another explanation, in the presence of aortic insufficiency, is that the regurgitant blood stream from the aorta forces the anterior cusp of the mitral valve backwards, producing a narrowing or stenotic-like effect of that valve. This is the usual explanation of the Austin Flint murmur.

Physiologic Effects

The physiologic effects of mitral valve disease vary with the type and degree of the valvular pathology. If the predominant lesion is stenotic and is marked enough, there will be interference with the free flow of blood from the left auricle into the left ventricle during diastole. This will result in increased left auricular pressure and in distention of that chamber, followed eventually by hypertrophy. There will also be an increase in the intrapulmonic vascular tension with distention and gradual development of sclerotic changes of those vessels. The right ventricle is thus put under greater strain, resulting ultimately in right ventricular hypertrophy. The left ventricle remains normal and may, in extreme cases, become smaller, due to decreased filling of that chamber because of the stenotic mitral valve.

If the predominant or the only effect of mitral valve disease is insuffi-

ciency, a certain amount of the blood entering the left ventricle during diastole is returned back to the left auricle during ventricular systole. There is thus a greater accumulation of blood in the left auricle and, therefore, a return of a greater amount of blood to the left ventricle during diastole The ultimate result is hypertrophy of the left ventricle and to some extent, also, of the left auricle. In severe grades of mitral insufficiency all the chambers of the heart become enlarged Heart failure in mitral insufficiency affects the left ventricle predominantly, but in severe cases, all chambers participate

Physical Signs

The essential physical findings in mitral valvular disease are the characteristic murmurs and changes in the size and shape of the heart These factors vary with the type and degree of valvular involvement

Signs of Mitral Stenosis Here, the *murmur is diastolic* in time. It is usually heard best at the apex or a little to the right and above and occasionally, in the fourth left interspace between the apex and the left sternal border. In mild cases, the murmur may only be heard on acceleration of the heart by exercise or amyl nitrite, and with the patient in the left lateral recumbent posture. The murmur is of low intensity and rumbling quality, and as such, it is best detected by the bell chest piece of the stethoscope. In some cases, a diastolic thrill is felt in the same area where the murmur is heard. The area of transmission of the murmur varies with its intensity In the average case, its transmission is usually localized to a comparatively small area In advanced cases, it may extend to the left sternal border and as far as the left anterior axillary line between the fourth and sixth interspaces. Figure 114 illustrates the location and transmission of the diastolic rumble of mitral stenosis, the direction of the blood flow through the stenosed mitral valve producing the murmur, and the changes in the configuration of the heart.

The intensity and the duration of the murmur vary with the degree of stenosis. This will be understood from the fact that under normal conditions, the blood flow from the auricles to the ventricles continues throughout the diastolic period, from the moment the auriculo-ventricular valves open and the semilunar valves close The greatest flow occurs in the early part of diastole when the accumulated blood in the auricles, during the period when the auriculo-ventricular valves are closed in ventricular systole, suddenly begins to fill the ventricles on the opening of these valves. This sudden rush of the accumulated blood from the left auricle into the left ventricle in early diastole, meeting some interference from the stenosed mitral valve results in a short early diastolic rumble.

In low grade stenosis, this short, early diastolic rumble, or in some cases,

an accentuated third heart sound is all that may be heard, because the flow of blood during the rest of diastole, being slower, will not be disturbed.

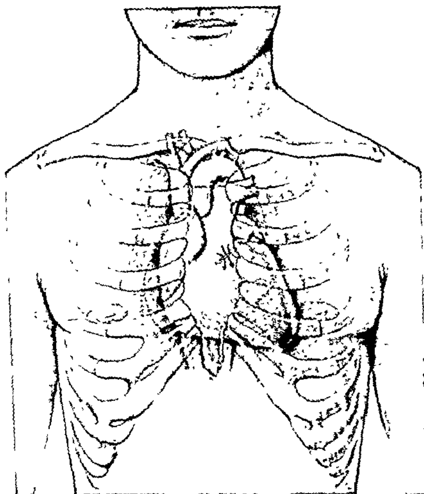


FIG 114 —LOCATION AND TRANSMISSION OF THE DIASTOLIC RUMBLE IN MITRAL STENOSIS, the direction of blood flow (arrows) producing the murmur and the change in the configuration of the heart Density of dots in different areas represents relative frequency of transmission of the murmur in those locations

This is often spoken of as the diminuendo type of diastolic murmur, shown in Figure 115

If the stenotic condition of the mitral valve is more marked, the early diastolic rumble is louder and may be continued in a milder intensity

throughout the rest of diastole, followed by increase in its intensity again immediately before the first heart sound. The increase in its intensity at this point is due to auricular systole which suddenly again accelerates the flow of blood towards the ventricle through the stenosed valve. The phase of such increase in the intensity of the murmur is often spoken of as the crescendo portion of the diastolic rumble. In advanced mitral stenosis, a markedly intense diastolic rumble occupies the entire diastolic period with, perhaps, some accentuation in early and late diastole. This is also true if the type of mitral stenosis is not marked but when the heart is rapid, result-



FIG 115—DIMINUENDO MURMUR IN LOW-GRADE MITRAL STENOSIS. It begins a short distance after the second sound and ends at a variable distance before the first sound of the next cardiac cycle. First sound, 1, Second sound, 2; Murmur, M.



FIG 116—LONG DIASTOLIC RUMBLE IN HIGH-GRADE MITRAL STENOSIS. It begins a short distance after the second sound and at the end of diastole it assumes a crescendo character merging with the first sound of the next cardiac cycle. First sound, 1; Second sound, 2, Murmur, M



FIG 117—DIASTOLIC RUMBLE OF MITRAL STENOSIS IN THE PRESENCE OF AURICULAR FIBRILLATION. The rumble varies with the ventricular rate and disappears before the first sound of the succeeding cycle. First sound, 1, Second sound, 2; Murmur, M.

ing in shortening of the diastole. Figure 116 illustrates the advanced mitral stenotic murmur in relation to the heart sounds.

With the onset of auricular fibrillation, the presystolic accentuation of the diastolic rumble disappears because the auricles do not contract normally. The rumble, therefore, diminishes as diastole proceeds, and finally entirely disappears before ventricular systole. Here again, the murmur varies with the ventricular rate and, therefore, with the degree of irregularity. If the rate is very fast, the diastolic rumble may last throughout each diastolic [illegible]

rumble, as shown in Figure 117.

To differentiate a mitral diastolic rumbling murmur heard occasionally in left ventricular dilatation, or in aortic insufficiency from organic mitral stenosis we must depend upon other signs indicative of mitral stenosis. These are an accentuated first sound at the apex, an accentuated and occasionally reduplicated second sound at the pulmonic area, enlargement of the *left auricle, right ventricle and pulmonary artery*, and an increase in the hilus shadow, demonstrated roentgenologically. The physical signs of right ventricular enlargment are a palpable precordial heave at the left of the sternal region, especially in the lower part, and an increase in the area of percussion dullness of the left upper border of the heart, as described in Chaper VI.

Signs of Mitral Insufficiency Here, the murmur is *systolic* in time. It is heard with maximum intensity at the apex Its area of transmission is mainly to the left and varies with its intensity If it is of low intensity, it is usually transmitted only to the anterior axillary line If more marked, it may be transmitted to the midaxillary line and to the back. In some cases it is also transmitted as far as the lower sternal region This is illustrated in Figure 118, which shows also, the abnormal direction of the blood flow through the defective mitral valve which causes the murmur, and enlargement of the left ventricle.

The mitral insufficiency murmur is usually of a blowing character and of fairly high pitch It may, however, assume a musical or grinding quality The loudness of the murmur is to some extent an indication of the degree of mitral insufficiency Where the insufficiency is extreme, the murmur may be hardly audible The duration of the murmur, likewise, varies in different cases, depending upon the degree of insufficiency, as shown in Figures 119, and 120 In some cases, a systolic thrill is felt in the same area where the murmur is heard

In well developed mitral insufficiency, we can demonstrate a varying degree of left ventricular, and also some left auricular enlargement In mild grades, however, left ventricular enlargement may be so slight as not to be demonstrable by physical or roentgenologic examination. In such cases, it may be difficult to differentiate the mitral insufficiency murmur from a nonorganic murmur In mitral insufficiency, however, the murmur is apt to be more constant, and does not, as a rule, change significantly with alteration in posture or respiration. However, it is better not to make the diagnosis of mitral insufficiency in the absence of some detectable left ventricular enlargement unless a definite history of rheumatic fever is obtainable

In relative mitral insufficiency, the murmur is usually of lower intensity than in organic mitral insufficiency. It occasionally displaces the first sound or if that sound is present, it is often of poor quality. There is always

considerable left ventricular enlargement present and there may be evidence of pulmonary stasis.

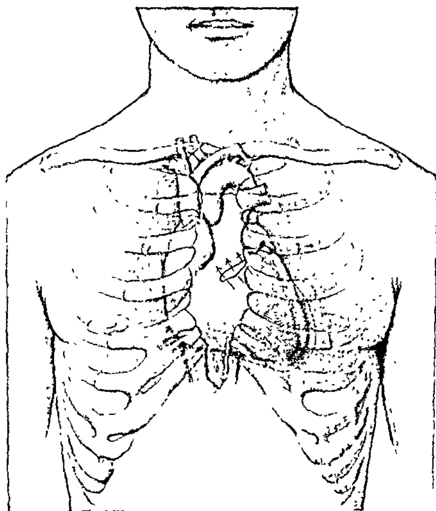


Fig. 118 —Location and Transmission of the Systolic Murmur in Mitral Insufficiency, the direction of the abnormal blood flow (arrows) producing the murmur and the change in the configuration of the heart Density of dots in different areas represents relative frequency of transmission of the murmur in those locations

In most cases of mitral pathology, there is clinical evidence of both mitral stenosis and insufficiency in different degrees. The characteristic murmurs will then be detectable

Complications

Mitral stenosis, if marked, will sooner or later result in right heart failure Before this occurs, the great majority of cases develop auricular fibrillation and in rare cases, auricular flutter which help precipitate such failure

In many cases, before the development of demonstrable heart failure, pulmonary congestion takes place and in some cases, a varying degree of hemoptysis may occur from time to time. In some cases, the hemoptysis may be very copious and serious.

The underlying cause of hemoptysis is probably marked pulmonary vascular stasis Ferguson and co-workers,[3] by special injection studies have demonstrated a direct venous connection between the bronchial and pulmonary veins in normal men of all ages In mitral stenosis, dilatation of the bronchial veins in the submucosa of the large bronchi occurs due to

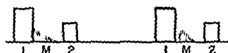


Fig 119—Systolic Murmur of Mitral Insufficiency, Low Intensity and Short Duration First sound, 1, Second sound, 2, Murmur, M



Fig 120—Systolic Murmur of Mitral Insufficiency Higher Intensity, Occupying the Entire Systolic Period First sound, 1, Second sound, 2, Murmur, M

stasis in the anastamotic pulmonary veins They believe that hemoptysis is due to ruputure of these bronchial vein varices.

Left auricular enlargement in mitral stenosis, if extensive enough, which is often the case, may compress the left lower bronchus and may result in stasis of the left lower lobe of the lung. This may occasionally predispose to secondary infection Cough may be an outstanding symptom The auricular enlargement may occasionally also compress the left recurrent laryngeal nerve, probably by pushing the left bronchus against the aortic arch This may produce some degree of vocal cord paralysis and hoarseness Figure 121 shows left auricular enlargement extending to the right border of the heart

An outstanding and very serious complication of mitral stenosis is the formation of mural thrombi in the left auricle which may serve as emboli. This is more apt to occur in the presence of auricular fibrillation but is often seen also in cases where the rhythm is regular. Cerebral embolization with

hemaplegia and symptoms of acute encepholomalacia, mesenteric embolization with intestinal gangrene, embolization to the abdominal aorta, at its bifurcation shutting off the blood supply to the lower extremities and pelvic organs and embolization to other parts of the body may often occur. These are the most trying cases.

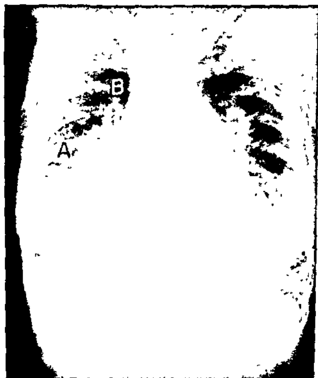


FIG 121 —CASE OF ADVANCED MITRAL STENOSIS The right border of the cardiac shadow is made up predominently of the left auricle, A, which is shown by a lesser density. The superior vena cava, B, and right innominate vein are distended The left bronchus assumes a more horizontal position From a female, 38 years old, presenting marked right heart failure

With the development of right heart failure, various complications may develop as a result of such failure as described in Chapter XIII. With marked right heart failure, some degree of relative tricuspid insufficiency may occur with signs to be described shortly.

A marked degree of *mitral insufficiency* may lead to early congestive failure with marked enlargement of all chambers of the heart, as shown in Figure 122.

A rare complication of a diseased mitral valve is sudden rupture of the

chordae tendineae which may occur under any strain or comparatively mild trauma. Bailey and Hickam[4] reported seven cases of spontaneous rupture with no history of strain. It should be suspected where there is a sudden appearance of a loud systolic murmur at the apex and left sternal border, associated with a thrill In some cases, an apical diastolic murmur may also develop. The condition may precipitate early congestive failure.

Subacute bacterial endocarditis affecting the mitral valve is another serious complication This is more apt to occur in mitral insufficiency.



FIG 122—MARKED DEGREE OF MITRAL INSUFFICIENCY WITH MODERATE STENOSIS AND EXTENSIVE CARDIAC ENLARGEMENT

DISEASE OF THE AORTIC VALVE

Pathology

The chronic fibrotic changes of this valve vary to some extent with the underlying etiologic factor and with the extent of the original acute process which caused the degeneration.

If the underlying cause was *rheumatic fever* and if the original inflammatory process was extensive, the cusps may become more or less adherent at their commissures resulting in a varying degree of stenosis In some cases, scarification of the cusps produces their retraction and stiffening and results in aortic insufficiency Nearly all cases have some degree of combined stenosis and insufficiency with predominance of one over the other.

A much greater number of these cases shows predominant insufficiency. In some cases, calcification of the valve may occur as in atherosclerosis.

In syphilitic involvement, commissural separation and some retraction of the cusps occur resulting in aortic insufficiency. Aortic stenosis does not occur in this disease

In *dissecting aneurysm* of the aorta, distortion of the aortic valve leaflets may occur and produce insufficiency, not stenosis, as shown in Chapter XXI.

In *atherosclerotic disease* of the aortic valve, the aortic ring is usually involved first, as said earlier in this chapter. As the process progresses, the valve cusps also stiffen and become deformed, producing in many cases stenotic changes Calcification often occurs, resulting in a varying degree of calcific aortic stenosis Some degree of insufficiency may also be present.

In *rupture* of the aortic valve *due to strain or trauma*, the tear may occur at the margin of the injured leaflet or at its base. Repetto and co-workers[5] believe that if caused by strain, the tear is at the angle of attachment of the leaflet, while in trauma, it is at the free margin Both of these conditions result in aortic insufficiency

Physiologic Effects

Aortic valvular disease alters the normal hemodynamics of the circulation. The extent and forms of alterations depend upon the amount and type of valvular damage. In mild grades, the alterations are insignificant, but in moderate and severe grades, they are marked. The forms of alterations depend upon the predominance of insufficiency or stenosis.

In pure or predominant *aortic insufficiency*, some of the blood leaving the left ventricle during systole flows back into that chamber during diastole. This blood added to the normal filling of the left ventricle by the left auricle during diastole results in a greater distention of the left ventricle During systole the left ventricle thus expels a greater volume of blood than normally, producing a greater distention of the aorta. Left ventricular hypertrophy and aortic dilatation consequently follow The extent of such hypertrophy and dilatation depends upon the degree of aortic insufficiency

Due to the increased filling of the aorta during systole, the systolic arterial pressure is increased Also, as a result of some backflow of blood from the aorta into the left ventricle and of reflex peripheral vasodilatation due to impulses arising from the distended aorta, there is a drop in the diastolic pressure. Thus, in well developed aortic insufficiency there is a high systolic and low diastolic arterial blood pressure resulting in a high pulse pressure. These pressure changes produce the characteristic peripheral vascular signs to be described shortly.

In pure or predominant *aortic stenosis*, the systolic discharge from the left

ventricle meets with obstruction. A greater burden is thus thrown on the left ventricle in expelling the blood. Concentric left ventricular hypertrophy follows. The blood enters the aorta with lesser force due to the obstruction so that the distention of the arterial tree is slow and of low amplitude The aorta, therefore, is not dilated, in fact it may be narrower than normal unless it has undergone some dilatation before the development of the aortic stenosis. The systolic blood pressure is usually low and the pulse is slowly rising and long sustaining, as described in Chapter X

Physical Signs

The signs of aortic valvular disease are those elicited from the examination of the heart and those from the peripheral vascular system The former are more important and may be present even in the milder grades where the peripheral vascular manifestations are either absent or are not clear cut.

The signs of aortic valvular disease vary with the type and degree of valvular involvement

Signs of Aortic Insufficiency Here, the *murmur is diastolic* in time and is usually of a soft, blowing quality and of high pitch Its maximum intensity, in most cases, is in the third or fourth left interspace close to the sternum or over the sternum itself at these levels. It may be transmitted to the apex and often also upwards and to the right as far as the aortic area When transmitted to the apex, it often diminishes in intensity between the fourth and fifth ribs and reappears with greater intensity again at the apex. In rare cases, it is heard best or only at the apex and it may then be differentiated from the murmur of mitral stenosis by its high pitch and soft quality and by the absence of other findings of mitral stenosis In some cases, the maximum intensity of the murmur is at the second and third interspace to the right of the sternum In rare cases, it may be loud and transmitted along the upper sternal region and left sternal border. This is more apt to occur in the coexistence of mitral stenosis

In traumatic injury of the aortic leaflets or where the leaflets are perforated by acute disease such as acute bacterial endocarditis, the murmur may be very loud, musical and widely transmitted throughout the anterior precordium as well as over the corresponding part of the posterior chest wall

Figure 123 illustrates the locations and radiations of the aortic diastolic murmur, and the abnormal direction of the blood flow through the defective aortic valve which causes the murmur. It also shows the resulting aortic dilatation and left ventricular enlargement.

At times, the murmur is of such low intensity as to be hardly audible. In such cases, it is best elicited by the diaphragm piece of the stethoscope, with

A much greater number of these cases shows predominant insufficiency. In some cases, calcification of the valve may occur as in atherosclerosis.

In syphilitic involvement, commissural separation and some retraction of the cusps occur resulting in aortic insufficiency. Aortic stenosis does not occur in this disease.

In *dissecting aneurysm* of the aorta, distortion of the aortic valve leaflets may occur and produce insufficiency, not stenosis, as shown in Chapter XXI.

In *atherosclerotic disease* of the aortic valve, the aortic ring is usually involved first, as said earlier in this chapter. As the process progresses, the valve cusps also stiffen and become deformed, producing in many cases stenotic changes. Calcification often occurs, resulting in a varying degree of calcific aortic stenosis. Some degree of insufficiency may also be present.

In *rupture* of the aortic valve *due to strain or trauma*, the tear may occur at the margin of the injured leaflet or at its base. Repetto and co-workers[5] believe that if caused by strain, the tear is at the angle of attachment of the leaflet, while in trauma, it is at the free margin. Both of these conditions result in aortic insufficiency.

Physiologic Effects

Aortic valvular disease alters the normal hemodynamics of the circulation. The extent and forms of alterations depend upon the amount and type of valvular damage. In mild grades, the alterations are insignificant, but in moderate and severe grades, they are marked. The forms of alterations depend upon the predominance of insufficiency or stenosis.

In pure or predominant *aortic insufficiency*, some of the blood leaving the left ventricle during systole flows back into that chamber during diastole. This blood added to the normal filling of the left ventricle by the left auricle during diastole results in a greater distention of the left ventricle. During systole the left ventricle thus expels a greater volume of blood than normally, producing a greater distention of the aorta. Left ventricular hypertrophy and aortic dilatation consequently follow. The extent of such hypertrophy and dilatation depends upon the degree of aortic insufficiency.

Due to the increased filling of the aorta during systole, the systolic arterial pressure is increased. Also, as a result of some backflow of blood from the aorta into the left ventricle and of reflex peripheral vasodilatation due to impulses arising from the distended aorta, there is a drop in the diastolic pressure. Thus, in well developed aortic insufficiency there is a high systolic and low diastolic arterial blood pressure resulting in a high pulse pressure. These pressure changes produce the characteristic peripheral vascular signs to be described shortly.

In pure or predominant *aortic stenosis*, the systolic discharge from the left

In some cases of marked aortic insufficiency, a short systolic murmur may be heard at the apex due to relative mitral insufficiency as a result of left ventricular enlargement. Also, a diastolic rumble resembling that of mitral stenosis may, at times, be heard at the apex, spoken of as the Austin Flint murmur, described in Chapter IX.

The *corroborative signs* of aortic insufficiency consist of left ventricular enlargement, aortic dilatation and certain peripheral vascular manifestations

Left ventricular enlargement varies with the degree of insufficiency from very slight to massive. *Aortic dilatation* affects predominantly the ascending portion, but the entire arch may be involved in advanced cases. Mild grades of aortic dilatation may best be visualized fluoroscopically, in the left anterior-oblique position, where a localized bulging of the ascending portion

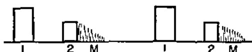


FIG. 124 —LOW GRADE AORTIC INSUFFICIENCY MURMUR It begins immediately after the second sound and ends long before the next first sound First sound, 1; Second sound, 2; Murmur, M



FIG 125 —HIGH GRADE AORTIC INSUFFICIENCY MURMUR, merging with the second sound and occupying almost the entire diastolic period First sound, 1, Second sound, 2, Murmur, M.

will be noted Such examination will also reveal an increased pulsation of the aorta and of the left ventricle

The *peripheral vascular manifestations* of aortic insufficiency consist of the Corrigan pulse, a high systolic and low diastolic blood pressure, capillary pulsation, the pistol shot sound, and the Duroziez sign

The *Corrigan pulse*, described in Chapter X, is a rapidly rising and rapidly [illegible]

imes

and

pistol

shot sound when we listen with the stethoscope over a large artery When the stethoscope is pressed more firmly, a to-and-fro murmur may be heard over the artery, known as the *Duroziez sign*

Capillary pulsation may be marked, and is elicited by slight pressure on the edge of a nail or by stroking the skin with the nail, producing dermographia This will be seen to redden and pale during systole and diastole respectively

All the above signs may be absent if a greater or less degree of aortic stenosis accompanies the insufficiency. They are also absent in the milder grades of aortic insufficiency, comprising about half the cases.

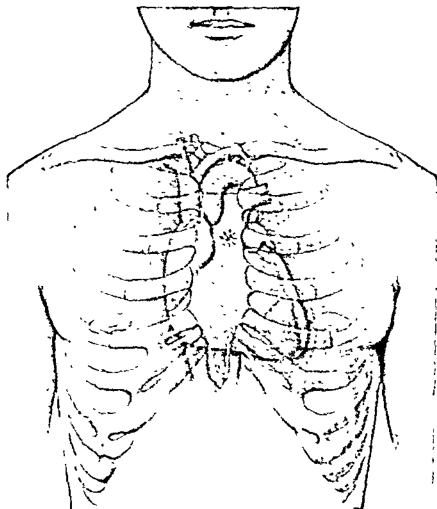


FIG. 126—LOCATION AND RADIATION OF THE SYSTOLIC MURMUR DUE TO AORTIC STENOSIS, *the direction of the blood flow (arrows) causing it and the resulting left ventricular enlargement.*

Signs of Aortic Stenosis Here, the *murmur is systolic* in time, and its maximum intensity is over the aortic area. It is usually rough, harsh and may be grinding in character. In calcific aortic stenosis, particularly, it may be extremely loud. The extent of its transmission is upwards to the right clavicle and to the vessels of the neck. It is often heard over both

clavicles, across the upper sternum and in some degree over the whole precordium as far as the apex. In occasional cases it may be very loud at the apex, and may thus be mistaken for a mitral insufficiency murmur. However, if traced upward and to the right, it will be found to diminish in intensity as we approach the left sternal border, but to become louder again as the aortic area is reached. A systolic thrill is often felt, especially at the aortic area Figure 126 illustrates the location and transmission of the aortic stenotic murmur, as well as the direction of the blood flow through the defective aortic valve. It also shows the associated left ventricular enlargement.

The duration of the murmur may be very short, occupying the early part of the systolic period, or loud, occupying the entire systolic period, burying the first heart sound which may not be audible, especially over the aortic area. In severe cases, the aortic second sound may also not be audible.

The position of the aortic stenotic murmur in relationship to the heart sounds is the same as that of mitral insufficiency, shown in figures 119 and 120.

The corroborative signs of well developed aortic stenosis consist of cardiac enlargement, absence of aortic dilatation and of the so-called pulsus parvus, tardus and rarus.

Left ventricular hypertrophy in aortic stenosis may be very marked and is mainly concentric. The aorta is not widened, unless it has undergone dilatation before the development of the stenosis It may actually be relatively narrower than normal

The so-called *pulsus parvus, tardus and rarus*, described in Chapter X, and the low systolic blood pressure may occur in advanced cases of the disease. These signs may be of help in differentiating the systolic murmur of aortic stenosis from nonorganic systolic murmurs often heard in the same area.

The differentiation of a systolic murmur heard at the aortic area due to dilatation of the ascending aorta from the murmur of aortic stenosis is based on the absence of hypertension, of aortic widening, and of the characteristic pulse of aortic stenosis Also, the murmur in aortic widening is usually much less intense and is not as widely transmitted as in aortic stenosis.

Complications

The main complication of aortic valvular disease is left heart failure, subacute bacterial endocarditis, occasionally auricular fibrillation and the anginal syndrome The last occurs more frequently in stenosis, than in insufficiency Syncope as well as sudden death are occasionally observed, as said before.

Disease of the Tricuspid Valve

Clinically recognizable disease of this valve alone is extremely rare. Its association with other valvular disease, however, is ocassionally observed.

All the above signs may be absent if a greater or less degree of aortic stenosis accompanies the insufficiency. They are also absent in the milder grades of aortic insufficiency, comprising about half the cases.

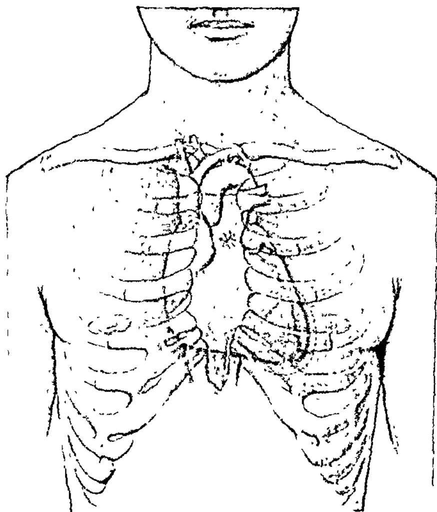


FIG 126.—LOCATION AND RADIATION OF THE SYSTOLIC MURMUR DUE TO AORTIC STENOSIS, the direction of the blood flow (arrows) causing it and the resulting left ventricular enlargement

Signs of Aortic Stenosis. Here, the *murmur is systolic* in time, and its maximum intensity is over the aortic area. It is usually rough, harsh and may be grinding in character. In calcific aortic stenosis, particularly, it may be extremely loud. The extent of its transmission is upwards to the right clavicle and to the vessels of the neck. It is often heard over both

clavicles, across the upper sternum and in some degree over the whole precordium as far as the apex In occasional cases it may be very loud at the apex, and may thus be mistaken for a mitral insufficiency murmur. However, if traced upward and to the right, it will be found to diminish in intensity as we approach the left sternal border, but to become louder again as the aortic area is reached. A systolic thrill is often felt, especially at the aortic area. Figure 126 illustrates the location and transmission of the *aortic stenotic murmur*, as well as the direction of the blood flow through the defective aortic valve. It also shows the associated left ventricular enlargement.

area In severe cases, the aortic second sound may also not be audible. The position of the aortic stenotic murmur in relationship to the heart sounds is the same as that of mitral insufficiency, shown in figures 119 and 120.

The corroborative signs of well developed aortic stenosis consist of cardiac enlargement, absence of aortic dilatation and of the so-called pulsus parvus, tardus and rarus.

narrower than normal

The so-called *pulsus parvus, tardus and rarus*, described in Chapter X, and the low systolic blood pressure may occur in advanced cases of the disease. These signs may be of help in differentiating the systolic murmur of aortic *stenosis from nonorganic systolic murmurs often heard in the same area.*

The differentiation of a systolic murmur heard at the aortic area due to

less intense and is not as widely transmitted as in aortic stenosis

Complications

The main complication of aortic valvular disease is left heart failure, subacute bacterial endocarditis, occasionally auricular fibrillation and the anginal *syndrome. The last occurs more frequently in stenosis, than in* insufficiency Syncope as well as sudden death are occasionally observed, as said before

Disease of the Tricuspid Valve

Clinically recognizable disease of this valve alone is extremely rare. association with other valvular disease, however, is ocassionally o

In a series of 173 cases collected by Osler and Gibson,[8] 100 cases were associated with mitral, 58 others with mitral and aortic and 3 with pulmonic valvular disease In only 12 cases was the tricuspid valve alone involved.

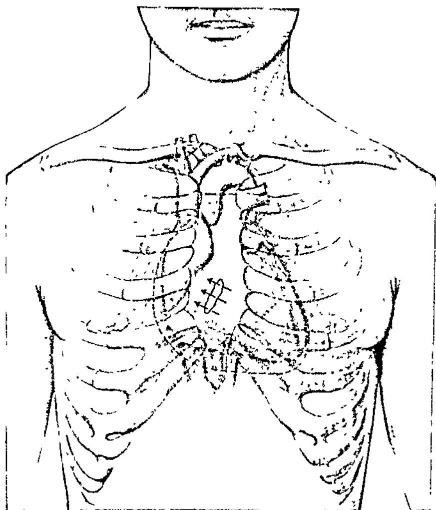


FIG 127—Location and radiation of the systolic murmur due to tricuspid insufficiency and the direction of the blood flow (arrows) causing it and the associated cardiac enlargement.

Pathology: Structural tricuspid insufficiency and stenosis present the same changes as similar conditions of the mitral valve. Relative tricuspid insufficiency may occur in association with right ventricular dilatation, in congestive failure.

Physical Signs: In *tricuspid insufficiency* the most important sign is the systolic murmur which is heard best at the xyphoid region. Often, however, it is impossible to differentiate it from a similar murmur transmitted from

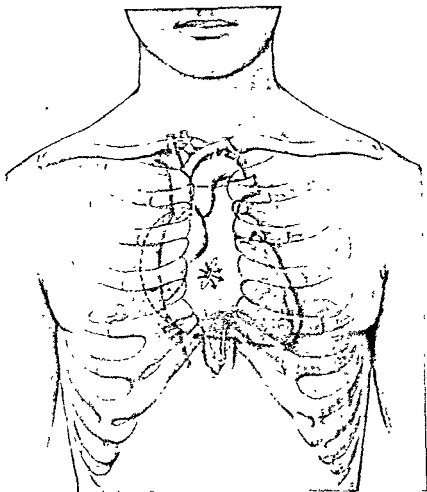


Fig 128 —Location and radiation of the diastolic murmur due to tricuspid stenosis and the direction of the blood flow (arrows) causing it and the associated cardiac enlargement

the apex in mitral insufficiency. Certain peripheral signs may help in the differential diagnosis. Thus, marked cyanosis of the face, and venous distention in the neck associated with some systolic pulsation of the veins and marked liver enlargment which shows systolic pulsations are in favor of

and no dilatation of the pulmonary artery unless other defects are associated with such stenosis. Relative pulmonary stenosis yielding a systolic murmur

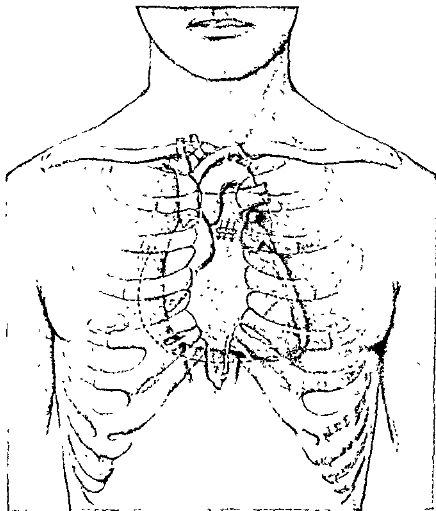


FIG. 130—LOCATION AND RADIATION OF THE DIASTOLIC MURMUR DUE TO PULMONIC INSUFFICIENCY, the direction of the abnormal blood flow (arrows) causing it, and the associated cardiac enlargement.

is associated with pulmonary artery dilatation, and factors that predispose to such dilatation.

In *pulmonary insufficiency* the murmur is diastolic in time, heard best at the pulmonic area, but is transmitted along the left sternal border and the midsternal region, as shown in Figure 130, which also illustrates the abnor-

mal direction of the blood flow through the tricuspid valve, and the resulting cardiac enlargement.

In the majority of cases where this murmur is heard, it is due to relative insufficiency of the pulmonic valve, rather than structural disease of that valve, as said before. Any condition that may increase the pressure in the pulmonary artery which causes its dilatation may be accompanied by this murmur, as described in Chapter XVIII.

In rare cases where a diastolic murmur of pulmonary valve insufficiency in association with intrapulmonic hypertension is due to mitral stenosis, it is labeled as the "Graham Steel murmur" after the author who first described it.[8]

A pulmonic insufficiency murmur may be difficult to differentiate from an aortic insufficiency murmur by the character or location of the murmur alone. The peripheral signs and the marked expansile pulsation of the aorta in aortic insufficiency, as well as the size and shape of the heart are the distinguishing differential diagnostic points.

Combined Valvular Disease

In many cases more than one valve may show clinical evidence of involvement in different degrees. The diagnosis of the valves affected and the type of involvement is made by careful auscultation of the given murmurs and their proper timing, as discussed above. In addition the size and configuration of the heart and great vessels, and the various peripheral signs mentioned under the respective valvular diseases, must be carefully determined to help arrive at a proper diagnosis.

Prognosis of Valvular Disease

The *prognosis of valvular disease* varies with the extent of damage, the [illegible]

In those cases where the valvular damage is slight and the etiologic factor that produced the damage is inactive and nonprogressive, the prognosis is good. The patient may attain a normal life span without any disturbance. This is true, however, only if the element of fear of heart disease is eliminated. Many of these cases suffer from a fear psychosis which is transformed into various somatic disturbances, after having been informed by the physician of the presence of heart disease. In children, this may result also in a serious inferiority complex, which may be carried on to later life. They develop the idea that they are not equal to the individual with a normal heart and there is the fear of impending danger. They are afraid to undertake any activity or any responsibility which may result in serious handicap.

In cases where the valvular damage is marked, and the etiologic element is progressive, such as in arteriosclerosis or in syphilis, or is recurring as in reactivation of a rheumatic process, the prognosis is much more serious. Here, the prognosis depends primarily on the rate of progress of the etiologic factor and upon the type of involvement. Thus if the etiologic factor is rheumatic fever and is frequently recurring, the valvular damage will be actively progressive and the life span may be short. This has been discussed in Chapter XXII If the etiologic factor is arteriosclerosis, the process is always progressive. However, the rapidity of progression, the valve or valves affected, and the type of affection vary in different cases and greatly influence the prognosis. As an example, in 78 cases of calcification of the mitral valve, reported by Fertman and Wolff[9] the average life span in those cases where only the annulus was involved was 69 years while in those where the leaflets were involved, only 44 years. In aortic valve stenosis and calcification, the average span of life in the series reported by Sophian[10] was 49 years

The economic status is an important factor which also governs the prognosis of chronic cardiovalvular disease. Those who are compelled to earn their livelihood by hard physical labor will develop congestive failure and die earlier than those who live a more leisurely life Also, improper hygiene, exposure to infections and poor nutrition lower the resistance of the patient and modify the prognosis

The development of subacute bacterial endocarditis changes the prognosis immediately In the past, the duration of life was only a matter of months after the onset of this complication With the use of penicillin and streptomycin in recent years, the immediate prognosis from this complication has greatly improved How much the ultimate prognosis will be modified by this therapy, however, is not as yet known.

The onset of auricular fibrillation or other arrhythmias, as well as the various complications, and congestive failure greatly change the prognosis Even here, however, many patients may go on quite comfortably for many years with modern therapeutic measures

Treatment

The treatment of chronic cardiovalvular disease is largely the treatment of the complications that may develop, such as the arrhythmias, congestive failure, subacute bacterial endocarditis, and the anginal syndrome These have been fully described under their respective headings. Uncomplicated valvular disease needs no treatment. Reassurance is essential and general hygienic measures employed in an attempt to prevent complications are necessary.

REFERENCES

[1] Marvin, H M, and Sullivan, A. G · Clinical observations upon syncope and sudden death in relation to aortic stenosis Am Heart J. 10 705, 1935
[2] Bland, E F, White, P. D, and Jones, T D. The development of mitral stenosis in young people Am Heart J. 10 995, 1935
[3] Ferguson, F C, Kobilak, R E, and Deitrick, J E. Varices of the bronchial veins as a source of hemoptysis in mitral stenosis Am Heart J 28 445, 1944.
[4] Bailey, O T, and Hickam, J B Rupture of mitral chordae tendineae, clinical and pathological observations on seven cases in which there was no bacterial endocarditis. Am. Heart J. 28 578, 1944
[5] Repetto, R, Ferrari, J A, and Benzecri, I Rupture of aortic valves due to effort. Prensa Med 44 2171, 1945
[6] Osler, W., and Gibson, A G Disease of the valves of the heart Modern Medicine, ed 2 Edited by Osler and McCrae, Vol IV, Chapter VIII Philadelphia, Lea & Febiger, 1915
[7] Rivero, C.. A new sign of tricuspid insufficiency Arch Inst Cardiol Mexico 16 531, 1946
[8] Steel, G.: Physical Signs of Cardiac Disease, ed 2 Edinburgh, 1881.
[9] Fertman, M H, and Wolff, L Calcification of the mitral valve. Am Heart J 31 580, 1946
[10] Sophian, L H · Calcific aortic valvular stenosis Am J M Sc 210 644, 1945

CHAPTER XXV

Disease of the Pericardium

THE PERICARDIUM may be affected by a variety of diseased such as congenital defects, diverticuli, neoplastic infiltration, el due to blood dyscrasias, avitaminosis, myxedema, transudations heart failure or in the form of hemopericardium due to trauma or ture of a chamber of the heart or a great vessel. All these conditi rare The most common pericardial disease is that of inflammation occasionally results in chronic fibrous pericardium with or without ca tion

Acute Pericarditis

Inflammation of the pericardium may be part of an acute panc or other acute cardiac insult or it may occur independently withou cardiac involvement

Etiology

The inflammation may be caused by rheumatic fever, various ki bacterial infection, uremia, myocardial infarction, trauma, and l comparatively rare condition of disseminated lupus erythematosis.

Of the bacterial infections, a great many organisms have been fo cause pericarditis, such as the pneumococcus, meningococcus, tu bacillus, streptococcus and so on. In some cases of so-called "idiop pericarditis, no specific organism can be found on repeated culture blood or pericardial fluid. Many of them are mild, some very s The author has recently observed a 38 year old male, presenting the form, associated with massive pericardial effusion and a septic tempe reaching, at times, as high as 106 degrees F The disease lasted weeks with final complete recovery. Repeated cultures of the bloo of the pericardial effusion yielded no organisms of any kind A guin inoculation gave negative results Cases of this kind are probabl to some virus infection.

The portal of entry of the organism or the focus of infection va [illegible]

rir

involved, and the associated meningococcus septicemia is responsib the pericardial involvement. In a series of 280 cases of epidemic men reported by Herrick,[1] 12 cases had an associated pericarditis.

Infection of the upper respiratory tract may be the primary source, as in the 8 cases reported by Nathan and Dathe.[2] Several other similar cases have been reported by other authors.

The focus of infection in tuberculous pericarditis may be a patch of pulmonary tuberculosis or rupture of a caseous lymph node or generalized miliary tuberculosis. Thompson[3] calls attention to the existence of primary tuberculous pericarditis. He quotes 21 cases from the literature and reports 7 cases of his own. All were elderly individuals, the youngest being 49 years, and the oldest 84, with an average age of 69 5 years His criteria for the diagnosis of primary tuberculous pericarditis are old age, unexplained cardiac failure which does not respond to treatment, a persistent, unexplained temperature and rapidly progressive fatal termination in a few months

Pathology

The *pathology of pericarditis* varies to a great extent with the etiology. The *gross appearance* of the rheumatic and infectious types is characterized by the deposition of an inflammatory fibrinous exudate, the thickness of which varies greatly with the severity of the disease and with the underlying infection. In some cases it may be as much as 1 cm. thick This exudate assumes a shredded "bread and butter" or villous appearance due to the constant movements of the heart This is the so-called dry stage A serous, and in some cases, a serohemorrhagic fluid may soon accumulate, the amount of which varies with the severity of the disease and with the underlying cause. In some cases, it may be as much as 2 or 3 quarts In cases where parts of the parietal and visceral pericardium become adherent, the accumulation of fluid in the free portions of the pericardial sack may produce localized bulgings, resembling aneurysms of the heart or basal vessels

Uremic pericarditis and pericarditis associated with a myocardial infarction seldom, if ever, result in effusion, and the amount of pericardial involvement is not marked

Pericarditis of rheumatic fever is never an isolated phenomenon, but is part of pancarditis, as discussed in Chapter XXII. Its presence here in a marked degree usually speaks for severe rheumatic cardiac involvement. In infectious pericarditis, the inflammation may involve a portion of the subjacent heart muscle In uremic pericarditis, the myocardium is not involved, but it may be the seat of degeneration due to arteriosclerosis.

Microscopically the appearance of the involved pericardium differs with the etiology, as pointed out by Porter[4] In rheumatic pericarditis, shown in Figures 109 and 110, the inflammation is the granular type, extending from the myocardium to the pericardium. In rare cases Aschoff bodies may be found In tuberculous pericarditis, Figure 131, the charac-

teristic tubercle is the outstanding feature. In pyogenic pericarditis, Figure 132, massive infiltration with polymorphonuclear lekcocytes is *the main feature* *In uremic pericarditis there are no inflammatory cells.* There is merely a layer of homogeneous material, which does not have the characteristics of fibrin, and appears to be a protein precipitate. It may contain eosinophiles



FIG 131.—TUBERCULOUS PERICARDITIS, SHOWING TYPICAL TUBERCLES, GIANT CELLS AND FIBROSIS OF THE VISCERAL PERICARDIUM There is some inflammatory reaction also of the subjacent myocardium × 68

In pericarditis, associated with myocardial infarction, there is a mild inflammatory reaction, some edema, round cell infiltration, with a thin layer of dense fibrin on the pericardial surface

Clinical Manifestations

These depend upon the severity of the underlying disease which produces the pericarditis, the degree of involvement of the pericardium; the presence

or absence of inflammatory changes in the structures adjacent to the pericardium, and, the amount of pericardial effusion.

Dry Pericarditis

This condition may be ushered in by an accentuation of the symptoms of the underlying disease which produced the pericardial involvement, although in some cases no accentuation of symptoms occurs In rheumatic



FIG 132—PYOGENIC PERICARDITIS Massive infiltration of the pericardium with polymorphonuclear leukocytes involving also the subpericardial layer of the myocardium × 100

pericarditis, the process is usually associated with an increase in temperature and a greater acceleration of the heart In septic pericarditis, due to an extension from pleuro-pulmonary disease, there is a continuation of, and often an increase in the temperature and septic symptoms incident to the original disease In the so-called idiopathic form or in tuberculous pericarditis, the condition may be ushered in with pain, high temperature, tachycardia, prostration, chills, and other septic symptoms

Pain often occurs in all forms of pericarditis, except in the uremic type. It is located mainly in the left precordium, but at times, it may occur in the left upper abdomen, in the suprascapular region or in the neck. On rare occasions it may radiate to the arms The pain may be continuous or intermittent, and is usually exaggerated by respiration. In many cases it is mild, but it may, at times, be so severe and sharp that the condition may be mistaken for acute surgical abdominal disease or for acute coronary occlusion.

Another, and more constant and definite finding of pericarditis sicca is the characteristic to-and-fro friction rub, described in Chapter IX. The friction rub may persist even with the accumulation of massive pericardial effusion

Pericarditis with Effusion

In those cases where a pericardial effusion develops, the clinical manifestations depend upon the amount and the rapidity of fluid accumulation. If the amount is small and accumulates slowly, there may be no symptoms. If the accumulation is large and occurs rapidly, so that the parietal pericardium has no time to undergo slow stretching, compression of the auricles, the venae cavae and the hepatic veins takes place. This interferes with the return of the venous blood to the heart and thus results in a diminished stroke and minute volume output. It manifests itself in more or less cyanosis and distention of the veins of the neck, increased venous pressure, enlargement and tenderness of the liver, tachycardia, fall in arterial blood pressure and diminished pulse volume.

If the fluid accumulation is extreme, compression of the lungs and mediastinal structures takes place in addition, and produces marked dyspnea with rapid, shallow breathing, a dry hacking cough, difficulty in swallowing, hoarseness, and the other symptoms mentioned above

Physical Findings Careful percussion will show a rapid increase in the area of cardiac dullness which may progress from day to day. The increased area of dullness is first noticed at the lower part of the heart region when the patient is in the sitting posture, and diminishes in the reclining posture There is also an increase in the area of dullness of the left upper portion of the heart region As the fluid accumulates, the area of dullness becomes more marked and extends also to the right.

The heart sounds may become muffled and diminished in intensity. The apical impulse may be felt in its normal position, some distance inside of the outermost point of cardiac dullness. Pulsus paradoxus, described in Chapter X, may be observed.

A very important sign of pericardial effusion is the presence of dullness and distant bronchial breathing over the left lower lung, posteriorly,

which is often mistaken for lobar pneumonia. This sign was first described by Ewart[5] and, therefore, bears his name. The dullness extends from the spine a variable distance towards the left, and as high as the ninth or tenth rib. If the effusion is marked, it extends over a wider area and may even reach a short distance to the right of the spine.

The differentiation of this area of dullness due to pericardial effusion from that due to pleural effusion in the left chest, as Porter[4] points out, is



FIG 133 — MASSIVE PERICARDIAL EFFUSION WITH MARKED LOCALIZED BULGING OF THE LEFT BORDER, SHOWN BY ARROW, RESEMBLING AN ANEURYSM OF THE LEFT VENTRICLE Also left and slight right pleural effusion For description of the case, see text

the absence of axillary flatness in the former, while in the latter, the highest point of flatness is in the midaxillary line

The electrocardiogram is an important aid in the diagnosis of pericarditis It is fully discussed elsewhere[6]

Roentgenologic Findings These vary with the amount of fluid. If small, there is bulging of the lowest corners of the heart shadow If the amount is large, the cardiac silhouette assumes the form of a water bottle with its sides sagging and resting on the diaphragm, if the x-ray is obtained in the standing or sitting position In the recumbent posture, the base becomes broader and the lower part narrower. Viewing the heart fluoroscopically,

there is marked diminution in the systolic pulsation of the left ventricle while the aortic pulsation is normal. This point is stressed by Berner.[7]

In some cases a localized collection of fluid may occur in various parts of the pericardium, as said before, due to pericardial adhesions and producing the appearance of an aneurysm, as shown in Figure 133.

This roentgenogram as well as those shown in Figures 134 and 135 are from a male, 32 years old, who developed pain in the right chest, radiating to the precordium and left shoulder associated with marked shortness of

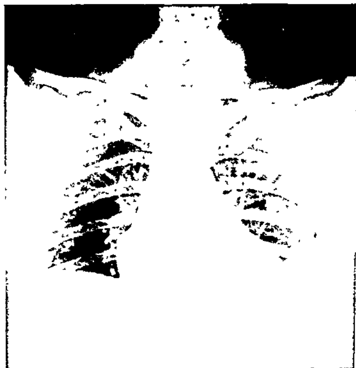


FIG 134—SAME PATIENT AS IN FIG 133, TWO WEEKS LATER Marked recession of pericardial and pleural effusion

breath He was confined to the hospital for over eight months with periods of quiescence and recurrence of activity During the quiescent periods he was practically symptom-free, and was afebrile. During the periods of recurrence, lasting two to four weeks, his temperature ranged between 101 and 104 degrees F, with marked dyspnea, recurring precordial oppression, and pain in the back of the neck, left shoulder and occasionally in the epigastrium There was marked tachycardia with diminished intensity of the heart sounds. Pleural and pericardial aspiration yielded a blood-tinged straw-colored fluid, containing many red cells,

a moderate number of lymphocytes, large mononuclear cells, but no tumor cells Although tubercle bacilli were not found and a guinea pig inoculation was negative after six weeks, the process was considered to be tubercular in origin, in view of its persistence, the character of the aspirated fluid, a repeated white blood cell count which was within normal limits, the absence of other bacteria on repeated culture of the fluid, and the presence of a highly positive tuberculin skin reaction He eventually

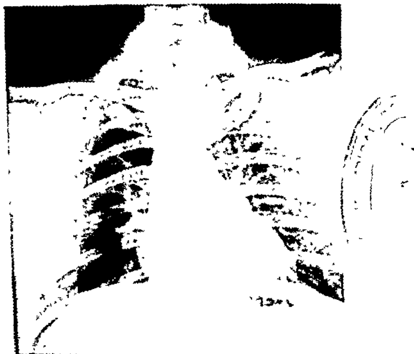


Fig 135 —Same Patient as in Figs 133 and 134, about Four Months after the Onset of Disease The heart shadow is within normal limits

made complete recovery after eight months of bed rest and six months of rest in a convalescent home

Figure 133, obtained about one week after the onset of his illness, shows massive pericardial effusion, with an area of marked bulging of the left middle portion of the cardiac silhouette which was interpreted by the roentgenologist as a possible ventricular aneurysm There is also moderate left pleural effusion Figure 134 was obtained about two weeks later It shows considerable recession of the pericardial as well as the pleural effusion Figure 135 was obtained about three and one-half months later. The cardiac shadow is within normal limits A number of other roent-

genograms obtained during his illness showed recurrences and recession of fluid accumulation.

Aspiration of the Pericardium: Pericardial tapping is very seldom necessary for therapeutic purposes and should not be resorted to unless the effusion is so massive as to threaten life In the vast majority of cases of rheumatic and other forms of pericarditis with effusion, the fluid is ultimately absorbed with the subsidence of the inflammatory process under complete rest. In tuberculous pericarditis occasional tapping may have to be resorted to in some cases because the effusion is more massive and tends to reaccumulate. Also a tapping may be necessary for diagnostic purposes This is particularly important in cases where the presence of pus is suspected or where the temperature is extremely high and septic symptoms are present This may also be necessary to establish the diagnosis of tuberculous pericarditis

There are several sites employed for paracentesis. The usual one is in the fifth or sixth left intercostal space within the area of cardiac dullness, but outside of the apex beat. Another one is beneath the junction of the enciform cartilage and the left costal arch. A third one is in the fourth right interspace just within the area of cardiac dullness. In occasional cases, where Ewart's sign is marked, we may employ the posterior route, inserting the needle in the left seventh or eighth intercostal space in the midscapular line, at the point of maximum dullness and bronchial breathing This route should not be chosen in purulent pericarditis as the infection may be spread to the lung and pleura.

The selection of the proper site requires a careful check on the area of the greatest bulge of the pericardium, determined by percussion and roentgenologic study. The patient should be in a sitting position An 18 or 16 gage needle is employed with a short point to prevent, if possible, any injury to the heart or coronary vessels. If the fifth left interspace is selected, the needle should be gradually inserted in an inward, backward and slightly upward direction, a distance of about 3 to 4 centimeters, depending upon the thickness of the chest wall. If the enciform route is selected, the needle is directed upward, backward and inward about the same distance. When the posterior route is employed, the needle is inserted to a depth of about 5 to 8 centimeters. In any position, the needle may have to be moved about slightly to obtain fluid. Occasionally a plug of fibrin in the needle may prevent the flow A stylet pushed through the needle may be of help. The area selected is to be fully anesthetized by novocain. In some nervous and restless individuals $\frac{1}{6}$ to $\frac{1}{4}$ grain of morphine is administered before attempting a paracentesis

Diagnostic Value of the Aspirated Fluid: Gross inspection and laboratory study of the aspirated fluid is frequently of great value in determining the

underlying cause of pericarditis. The laboratory study should include a determination of the physical characteristics, the cellular content, and the bacteriology of the fluid.

A serous or serofibrous fluid suggests the presence of a rheumatic or so-called idiopathic or virus pericarditis. A serohemorrhagic fluid may indicate tuberculous pericarditis, malignancy and traumatic injury A seropurulent or purulent effusion speaks for pyopericardium

Microscopic findings of a great preponderance of polymorphonuclear leukocytes in a well preserved or deformed state, speak for infectious pericarditis. The preponderance of small lymphocytes together with a few monocytes and very few polymorphonuclear neutrophils suggest a tuberculous process

A bacteriologic study by smear and culture may determine the organism in most cases of infectious pericarditis. Occasionally a nonhemolytic streptococcus may be obtained from fluid in rheumatic pericarditis In about 30 per cent of cases of tuberculous pericarditis the tubercle bacillus may be obtained from the fluid In many other cases a guinea pig inoculation will yield a positive result It is important to remember that occasionally a guinea pig inoculation will not show evidence of the infection for several months, as in the case reported by Barrett and Cole [8] Hence the animal should be observed for a long time before the test is considered negative

Prognosis

The outcome of pericarditis varies with the underlying disease, and with the severity of the pericardial involvement The tubercular form carries a serious prognosis In many cases it ends in death, and those who survive are often left with massive pericardial adhesions and calcification The rheumatic form may subside and leave very little residue, although if severe, it may also leave massive adhesions The so-called idiopathic form usually clears entirely, leaving no adhesions This is true, especially, of the milder grades Purulent pericarditis was almost always fatal previously Of late, the use of penicillin has greatly improved its prognosis

The amount of fluid that accumulates in the pericardium may modify the prognosis of the underlying disease which produces the pericarditis

Treatment

In all cases of pericarditis the most essential therapeutic measure is complete bed rest until all signs of activity subside. If pain is an outstanding feature, codeine, and if very severe, morphine will have to be used Local application of an ice bag may also give relief in some cases. If restlessness is marked, the barbiturates or demarol may offer relief. If effusion accumulates and breathing is difficult, the sitting posture will afford some relief.

In rheumatic pericarditis the treatment is that of rheumatic fever, described in Chapter XXII

In purulent pericarditis, the use of penicillin intramuscularly, also aspiration of the purulent fluid and injection of 10,000 to 20,000 units of penicillin in 10 to 30 cc of saline solution in the pericardial cavity, as suggested by Wise and Shafer,[9] may cure the condition. If not, surgical drainage will be necessary.

In the so-called idiopathic pericarditis symptomatic relief and patience are essential in its successful therapy. Penicillin or streptomycin in large doses may be tried for several days If the course is not altered, further continuance of such drugs is useless and is an additional annoyance to the patient

In tuberculous pericarditis prolonged bed rest, symptomatic relief and aspiration of the pericardial effusion, if it becomes extremely distressing, are all that can be offered. Streptomycin may be tried, but is not to be continued if it does not show a definite therapeutic effect, as the author's limited experience would indicate

When a therapeutic aspiration of pericardial effusion is done, it is essential not to withdraw all the fluid at once However, enough should be withdrawn to give great relief from dyspnea and other distressing symptoms

Chronic Fibrous Pericardium

Fibrosis of the pericardium may result from pre-existing inflammation, described under acute pericarditis The underlying causes, therefore, are those of acute pericarditis mentioned before Inasmuch as the pathology, in its fully developed state, consists of fibrosis and not of active inflammation, the term "fibrous pericardium" is preferred to that of "chronic pericarditis" often used.

Pathology

Fibrosis of the pericardium may consist merely of very slight scarring, or it may be so extensive as to obliterate the entire pericardial cavity and extend extrapericardially to the pleura, diaphragm, ribs and involve the mediastinum Between these two extreme degrees there is a variety of gradations and areas of involvement

From a clinical viewpoint, we may divide the disease into three groups In one, the fibrous bands are loose and do not interfere with the normal functioning of the heart These cases are usually not recognized during life, and are discovered at autopsy.

In another, there are massive and firm adhesions between the parietal

and visceral pericardium, which is often incrustated with a considerable amount of calcium The adhesions may be so tight that they produce marked constriction of the heart and interfere in its function. Because the thinner right chambers under such circumstances cannot dilate properly during diastole, filling of the heart by the venous return is incomplete and thus the stroke and minute volume output is diminished. Chronic venous stasis is the result The condition is often spoken of as *concretia cordis* or *chronic constrictive pericarditis*. The heart in such cases is usually of normal size or even smaller than normal. It is often also accompanied by considerable extrapericardial adhesions to the chest wall and diaphragm.

In a third group may be included cases where the extrapericardial adhesions are very extensive, involving the entire mediastinum, the diaphragm and the adjacent bony structures of the chest. It may produce constriction of the superior and inferior venae cavae and the hepatic veins. The condition is spoken of as *chronic adhesive mediastinopericarditis*. When the constriction produces obstruction of the inferior vena cava and hepatic vein, chronic hepatic stasis occurs and results in marked enlargement and cirrhosis of that organ Pick[10] attempted to differentiate this form of secondary hepatic cirrhosis from primary cirrhosis of the liver He named the condition *mediastinopericarditic pseudocirrhosis of the liver* which is since known as "Pick's disease" Ascites, polyserositis and perihepatitis as well as splenic enlargement with perisplenitis often accompany the cirrhosis

The heart, in this group, may be greatly enlarged due to the pull by the adhesions and in some cases also to associated valvular disease.

Clinical Manifestations

These depend upon the degree of interference with the normal physiologic function of the circulation If there is no interference, the condition is asymptomatic. If there is moderate interference, there may be some dyspnea, cyanosis and slight distention of the veins of the neck on exertion, not unlike that seen in early congestive heart failure Prolonged interference may even produce liver enlargment These symptoms are due to accelerated venous flow to the heart during exertion which cannot be taken up by the heart. The dyspnea is due to some degree of anoxia, for the acceleration of the heart, occurring on exertion, in these cases, does not increase the stroke and minute volume output as was recently shown by Lyons and Burwell.[11]

Where the mechanical constriction is extreme, the clinical symptoms and signs depend upon the area of greatest interference with the return venous flow.

Massive chronic pericardial pathology with calcification may exist in some cases with absolutely no symptoms. It may be discovered accidentally in the course of examination, as exemplified by the following case:

A male, 68 years old, developed an upper respiratory infection of two weeks' duration. In the course of the examination, teleoroentgenograms of his chest, shown in Figures 136 and 137, revealed massive pericardial calcification. There was nothing in his past history to indicate any preexisting disease that could predispose to pericarditis. He was foreign

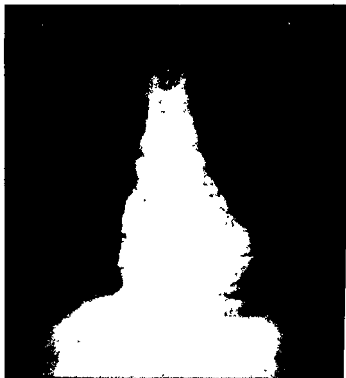


FIG. 136—ANTERO-POSTERIOR VIEW OF THE HEART SHOWING MASSIVE PERICARDIAL CALCIFICATION.

born, and worked all his life from his early youth, in a factory as a leather goods cutter, never having been debilitated by any disease. He could not recall any serious illness in early childhood, although he remembered having been told by his mother that he had had some sickness in early infancy

Physical examination of his heart failed to reveal any evidence of disease. There was no cardiac enlargement. The heart rate was 72, the rhythm regular, the heart sounds were normal and no murmurs were heard. There were no signs of any cardiac embarrassment, but there was some electrocardiographic evidence of myocardial damage.

The only clue to a possible cause of the chronic pericardial involvement was the presence of calcification of the apex of the right lung and some dilatation of the pulmonary artery. This would suggest that the underlying cause was pre-existing pulmonary tuberculosis from which he suffered in early childhood, and which was associated with tuberculous pericarditis, followed by organization and calcification.



FIG 137—SAME PATIENT AS IN FIG 136 IN THE LEFT ANTERIOR OBLIQUE VIEW For case history, see text

In some cases the condition is associated with cyanosis, venous distention of the neck, increased venous pressure, marked liver enlargement, ascites, abdominal distress and dyspnea. Severe paroxysmal nocturnal dyspnea or orthopnea never occur here.

Physical examination fails to reveal any cardiac enlargement, usually seen in heart failure. This is one of the most important differential diagnostic points. Another confirmatory finding is the absence of demonstrable valvular disease. The pulse may be of somewhat lower amplitude

than normal and *pulsus paradoxus* is frequently observed. The arterial pressure is usually normal, but in some cases it may be lower than the average normal.

A very important point in the *differential diagnosis* of this condition from congestive failure is the therapeutic test Heart failure is improved by digitalis and the various diuretics, while in constrictive pericarditis the response to such therapy is poor. The venous pressure remains elevated and the liver enlargment and ascites remain about the same There may be slight temporary improvement at times

The diagnosis of this condition is often helped by a roentgenologic examination. The size of the cardiac silhouette is normal, but there may be some irregularity of the cardiac shadow due to small accumulation of fluid in localized free areas of the pericardial cavity. Calcification of the pericardium may be observed and may, at times, be very extensive. Fluoroscopically, there is diminished amplitude of cardiac contraction.

Chronic Pericardio-Mediastinal Adhesions

If the venous return is interfered with by adhesions in this condition, the clinical course is the same as in constrictive pericarditis, discussed above. However, here the heart is anchored to the chest wall and diaphragm, and is exposed to greater strain during systole because of a constant pull by the heart on the relatively non-yielding structures Progressive dilatation of the heart chambers, therefore, ensues, followed by hypertrophy. In contradistinction to that of the intrapericardial constrictive type, where the heart is small, here the heart is enlarged Because of dilatation of the ventricles and the auriculo-ventricular rings, signs of mitral insufficiency may be present. The condition is also often associated with structural valvular disease

Another point in the differential diagnosis of this condition is the occurrence of retraction of the intercostal spaces around the apical region of the heart and below the angle of the left scapula, during systole. Broadbent[12] called attention to such retraction in the latter location, and the sign is, therefore, named after him.

A third differential diagnostic point that may be observed is the immobility of the heart with change in the position of the body. As pointed out in Chapter V, *normally the apical region of the heart shifts 2 or more centimeters* to either side on change from the dorsal recumbent to one or the other of the lateral recumbent positions of the body. In this condition, no definite change in body position of the apex can be demonstrated on change in body position, due to the adhesions.

The roentgenologic findings of cardiac enlargement with occasional

irregularity of the cardiac silhouette and no descent of the heart during inspiration due to adhesions may help to confirm the diagnosis.

We must bear in mind the fact that marked cardiac enlargement, due predominantly to dilatation, especially in thin chested individuals, may simulate all the signs of massive pericardial adhesions, even the Broadbent sign In the presence of cardiovalvular disease or hypertension and arteriosclerosis with signs of congestive failure, the diagnosis of adhesive pericardium should not be definitely made even if the signs suggest the presence of the condition

Prognosis

Individuals presenting the nonsymptomatic form of pericardial adhesions may go through life and reach an old age, with practically no disturbances, as in the example given above The condition may be discovered accidentally or on autopsy and it may frequently be impossible even to trace the origin and cause of the fibrosis Patients with the symptomatic form of the disease usually go through a life of invalidism and die before middle age from chronic circulatory disturbances, hepatic disease or from intercurrent infection

Treatment

The asymptomatic group requires no treatment The symptomatic group can not be successfully managed medically, but often requires surgical interference This consists either of the removal of several ribs and costosternal cartilages or more extensive removal of the adhesions and part or all of the pericardium Both require skilled surgery. The choice of operation depends upon the type and extent of involvement and the condition of the patient Proper surgical and medical judgment must be employed in the individual case

REFERENCES

[1] Herrick, W W Meningococcic pericarditis with report of twelve cases Med Clin. North America 2 411, 1918
[2] Nathan, D A, and Dathe, R A Pericarditis with effusion following infections of the upper respiratory tract Am Heart J 31 115, 1946
[3] Thompson, W P Primary tuberculosis of the pericardium J.A M.A 100 642, 1933
[4] Porter, W B Acute pericarditis in the diagnosis and treatment of cardiovascular disease Editor Stroud, W E Philadelphia, F A Davis Co, 1 288, 1940
[5] Ewart, W Practical aids in diagnosis of pericardial effusion in connection with the question as to surgical treatment Brit M J 1 717, 1896
[6] Sigler, L H The Electrocardiogram, Its Interpretation and Clinical Application New York, Grune & Stratton, 1944 Pp 302–310
[7] Berner, F Ein neues Rontgensymptom bei Herzbeutelergub Fortschr a d Geb d Roentgenstrahlen 56 536, 1937

[8] Barrett, A M , and Cole, L A case of tuberculous pericarditis. Brit Heart J 6 185, 1944
[9] Wise, A. W , and Shafer, L E Purulent pericardial effusion treated with penicillin given intrapericardially J.A M A. 127 583, 1945
[10] Pick, F Uber Chronische unter den Bilde der Lebercirrhose Verlaufende Pericarditis (Perikarditische Pseudolebercirrhose) Nebst Bemerkungen über Zukkergussleber Ztschr. f. Klin Med. 29 385, 1896.
[11] Lyons, R H , and Burwell, C S Induced changes in the circulation in constrictive pericarditis Brit Heart J. 8 33, 1946
[12] Broadbent, J F H . Adherent Pericardium. London, 1895

CHAPTER XXVI

Disease of the Myocardium

THE HEART muscle, like other parts of the body, may be subject to inflammation, degeneration, trauma, neoplastic changes, metastatic malignant infiltration and parasitic invasion. Any of these pathologic changes, if marked enough, may interfere with its normal contraction and result in a variable degree of failure.

We shall review here, briefly, the more common pathologic processes affecting the heart muscle.

MYOCARDITIS

Definition. The term myocarditis is often used to describe acute parenchymatous degeneration as well as acute interstitial inflammation of the myocardium The two processes in the majority of cases occur together in various degrees In some instances, however, there may be very little, if any, parenchymatous changes while the interstitial inflammation may be marked In others, there may be marked acute parenchymatous degeneration without interstitial cellular reaction.

It is, therefore, perhaps better to designate the first as acute interstitial myocarditis, and the second as acute myocardial degeneration.

Etiology: Interstitial inflammation of the myocardium occurs most frequently in rheumatic fever, but it may also occur in various other infectious states In a review of 1,420 general autopsies in children, 8 days to 16 years of age, Saphir and co-workers[1] found the incidence of myocarditis to be 6 83 per cent. The various diseased states in which myocarditis was found were meningitis, poliomyelitis, bronchopneumonia, lobar pneumonia, nephritis, bacterial endocarditis, rheumatic fever, tuberculosis, and various other infections.

Gore and Saphir[2] have observed 35 deaths from acute nasopharyngeal and tonsillar infections where acute myocarditis was found at autopsy. In only 3 of these was heart disease suspected during life. In 4 cases where electrocardiograms were obtained, there were abnormal configurations of the complexes They believe that myocarditis is not uncommon in such infections.

Wendkos and Noll[3] report a case presenting abnormal electrocardiographic changes during epidemic parotitis and quote Pujol who reported 3 cases, and Manica who cited 1 case with postmortem findings.

Finland and co-workers[4] report 2 cases of acute myocarditis due to in-

fluenza A infection, and review the literature of many other cases Most of the reported cases have occurred during convalescence, and sometimes, long after the apparent recovery. In 1 case, the duration of the myocarditis was probably two to four weeks and death resulted from cardiac failure. In the second case, the duration of the disease was six to nine days. The influenza A virus was isolated from the lungs in both cases.

There is a comparatively rare form of acute interstitial myocarditis of unknown etiology with a clinical picture of progressive cardiac failure. It is not preceded or accompanied by an infectious disease The condition



FIG 138 —ACUTE INTERSTITIAL MYOCARDITIS ASSOCIATED WITH PNEUMONIA, IN AN INFANT

was first fully described by Fiedler[5] in 1899 and is, therefore, often labeled as "Fiedler's myocarditis," although several cases had been reported by other authors before him In a case reported by Bailey and Andersen,[6] the condition simulated coronary occulsion These authors believe that pyogenic infection of the skin may be the underlying cause Various other sources of infection have been suggested by other authors.

Saphir[7] observed 8 instances of myocarditis occurring in 152 cases of *bronchiectasis*. In 3 of these, sudden unexpected death occurred. He believes that the condition may be a contributing cause of sudden death in asthma.

Pathology: In well-advanced cases, the heart chambers are dilated, the muscle being soft, pale and flabby.

Microscopically, acute interstitial myocarditis is characterized by infiltration of lymphocytes, eosinophiles, polymorphonuclear leukocytes and histiocytes in the perivascular connective tissue and between the muscle fibers. The cellular content varies to a great extent with the causative factor. In severe pyemic infections, the collections consist of polymorphonuclear leukocytes and may be so great as to form multiple focal abscesses, and in rare cases the abscesses may be seen with the naked eye. Figure 138 shows acute interstitial myocarditis

In the rare form of tubercular myocarditis, miliary tubercules may be found in different parts of the myocardium. In very rare cases large caseous areas may be present.

Clinical Manifestations In many cases the outstanding clinical manifestations are those of the underlying disease and the coexisting myocardial involvement may be overlooked. On the other hand, the presence of abnormal signs referable to the heart in the course of some infectious disease may not always indicate that myocarditis is the cause For instance, fever, tachycardia, some of the arrhythmias, together with leukocytosis and increase in the erythrocyte sedimentation rate are frequent occurrences in infection, whether or not the heart is involved Even a systolic murmur may occur under such conditions in the absence of structural cardiac disease To make a diagnosis of myocarditis in any acute infectious state, we must have more specific evidence of myocardial involvement Of course, if myocarditis occurs after the active infectious state has subsided, the recurrence of the above evidence of infection may be of help in diagnosis This is particularly true of so-called Fiedler's myocarditis, where the condition is not associated with a known infectious disease

The most important clinical evidences of the presence of structural myocardial involvement are: (1) changes in the character of the first heart sound, which may become very weak or short, and may assume a valvular quality, (2) the development of marked tachycardia, far out of proportion to temperature, as well as one of the severe arrhythmias; (3) the occurrence of a gallop rhythm, (4) the development of progressive enlargment of the heart associated, at times, with a mitral insufficiency murmur; and (5) the onset of signs of cardiac failure. These are all fully described in previous chapters Significant rapid progressive changes in the electrocardiogram help to confirm the diagnosis. These have been described elsewhere [8]

Inasmuch as these manifestations may occur in any myocardial disease

besides myocarditis, we must rule out all other conditions and must have evidence of an infectious agent, to make a positive diagnosis of myocarditis.

The diagnosis of *chronic myocarditis* is much more difficult to make. The term implies the continuation of low grade inflammatory changes in the heart muscle over a long period It is a rare condition and the diagnosis should not be made in individuals of the arteriosclerotic age unless there is an underlying cause for inflammation. The term chronic myocarditis, often used in cases of myocardial fibrosis due to any cause, is erroneous, and gives us a wrong conception of the underlying pathology.

Myocardial Degeneration

Myocardial degeneration may be acute or chronic. Acute degeneration consists of various pathologic changes of the muscle fibers and is usually associated with more or less cellular reaction in the interstitial tissue, as said before Chronic degeneration consists of myocardial fibrosis which is the final stage in repair of all injured heart muscle In rare cases, there may be some calcification

Acute Parenchymatous Degeneration

Etiology· The underlying causes are various toxins, poisons and nutritional disturbances of the heart muscle

Of the toxins, diptheria is the best known example Many of the deaths from diphtheria are due to destruction of the myocardial fibers by the diphtheria toxin The interstitial changes in the acute, fatal cases may be minimal

Acute degenerative changes of the myocardium have also been observed on rare occasions in fatal cases of hyperthyroidism, avitaminosis, trichinosis and myxedema.

The various poisons that are known to affect the myocardial parenchyma are carbon monoxide, phosphorous, potassium chlorate and arsenic in lethal doses The heart, under such conditions, is affected like other parts of the body.

The most important and most common cause of parenchymal myocardial destruction is coronary sclerosis and occlusion. The pathologic changes in such cases, however, are more massive, more localized and vary grossly in many respects from the other types of degeneration, as described in Chapter XX

Pathology· Grossly, the heart in acute parenchymatous degeneration is similar to that of acute interstitial myocarditis, as said before. Micro- [illegible] ion of the
are more
ations are

lost and, in severe cases, the fiber assumes a waxy appearance. In some cases, only portions of the fiber may undergo such changes. A varying degree of reactive inflammatory changes with cellular infiltration of the adjacent interstitial tissue occurs in those cases where the patient does not die very early in the disease. If he survives long, many of the areas undergo fibrotic changes.

In severe anemia, fatty degeneration of the muscle fibers may occur. It must be differentiated from fatty infiltration of the interstitial tissue of the heart, which may occur in marked obesity, and represents simply a deposit of fat cells, the same as in the pericardium and other tissues throughout the body. If infiltration of the heart muscle is extensive, however, the clinical effects may be the same as in fatty degeneration, although milder in degree. Interstitial edema in the myocardium may be observed in many cases of acute degeneration.

Clinical Manifestations The clinical manifestations are predominantly those of the underlying disease which causes the myocardial degeneration. Symptoms referable to the heart may be overlooked and are the same as those of acute myocarditis

Treatment: In acute myocarditis and myocardial degeneration this concerns the management of the underlying disease Continuous bed rest is most essential until all signs of infection subside Penicillin and streptomycin are to be used in those infections which respond to such therapy. Other medication should be entirely symptomatic

In diphtheria, it is most essential to treat the disease by antitoxin early, in an attempt to prevent cardiac involvement. If such involvement has already occurred, the only therapy we have is *absolute bed rest* until all signs of activity have subsided Sudden death may occur if the patient is allowed to sit up or get out of bed before the acute process has entirely subsided If the myocardial involvement is marked, the prognosis is very grave and death may occur even at bed rest.

If signs of congestive failure develop in the course of myocarditis digitalis may be tried, although the response is usually poor in cases where actual inflammatory or degenerative changes of the heart are present Signs of digitalis toxicity often exhibit themselves under such circumstances before any therapeutic value is derived from the drug

Chronic Degeneration

This consists of fibrosis of the myocardium which represents the final stage of repair in the process of inflammation, acute degeneration, infarction and traumatic injury. The extent of fibrosis varies with the original underlying pathologic process. In occasional cases, the etiology

is not known, as in those reported by Smith and Furth,[9] Reisinger and Blumenthal[10] and others.

The most common cause of fibrosis of the myocardium is coronary sclerosis and occlusion, resulting in myocardial infarction. Here the fibrosis may be widespread, involving some parts of the heart muscle more than others To the naked eye, the fibrosed areas appear as white or gray strands, or localized scars In occasional cases of cardiac hypertrophy due to hypertension or other causes, some degree of fibrosis may occur even if coronary sclerosis is slight or moderate in degree

Microscopically, fibrosis following myocardial infarction is characterized by its localization in the muscle substance in contradistinction to that following interstitial myocarditis where its localization is perivascular and *in some cases in the form of narrow streaks in the interstitial parts of the* myocardium.

Calcification of the Myocardium

As a primary manifestation, calcification of the myocardium is extremely rare, if it occurs at all. In severe osteoporosis and in hyperparathyroidism it may rarely occur as a metastatic manifestation In all other conditions deposition of calcium almost invariably takes place only in previously damaged areas of the heart.

Brown and Evans[11] found 14 instances in the literature and report one case of their own where the condition was supposedly primary. Inasmuch as most of these cases had coronary disease, they cannot actually be so considered Diamond[12] reported a case of massive degeneration and calcification of the myocardium in a 26 week old premature infant, which he thought was due to some unknown toxic condition Edelstein[13] recently reported a case of an 11 year old boy with massive calcification and bone formation in the myocardium He believed that necrotizing lesions of the muscle due to diphtheria or some infection might have been the underlying cause.

Atrophy of the Myocardium

Brown atrophy of the heart muscle may occur in any severe and prolonged debilitating disease, in starvation and in senility. It is characterized by *a diminution in the size of the heart and a deposition of pigment* in the cell substance. Roberts and Beck[14] have also observed atrophic changes of the heart muscle in chronic constrictions of the heart, such as occurs in constrictive pericarditis, and they have reproduced the condition experimentally in dogs. They believe that circulatory failure in constrictive pericarditis is due mainly to myocardial insufficiency caused by atrophy, not to the adhesions themselves They, therefore, feel that

operation on the bony pericardium or phrenic nerve in patients with compressed hearts is of no value.

Trauma of the Myocardium

Trauma of the myocardium may be caused by penetrating and nonpenetrating chest injuries. The former may consist of stab wounds, bullet wounds or of fractured ribs penetrating the heart muscle. Nonpenetrating injuries may be caused by a severe blow to the chest, or severe compression antero-posteriorly, or by the transmission of an indirect traumatic force to the heart from other parts of the body caused by a fall from a great height, or other severe accidents.

The pathologic changes in the myocardium vary with the form of injury. Penetrating chest injuries may result in laceration of heart muscle with or without complete penetration of the wall In incomplete penetration, and where no coronary vessel was cut, the sectioned heart muscle fibers undergo degeneration followed by repair in the form of fibrous replacement. In complete penetration of the ventricular or auricular wall, or where a large coronary vessel is severed, severe hemorrhage and pericardial tamponade may occur, resulting in death

Nonpenetrating chest injuries, if severe enough, may also produce rupture of any of the chambers of the heart or of a valve. If not very severe, contusions and abrasions of the heart muscle may occur. Coronary thrombosis may follow in some cases The subject has been fully discussed before [8 15 16]

Cardiac Aneurysm

Localized aneurysmal dilatation of the heart may develop in any condition where massive local myocardial fibrosis is present. It is produced by intraventricular pressure which gradually stretches and distends the yielding fibrosed region Inasmuch as the largest areas of fibrosis occur as a result of massive infarction, the vast majority of cases of cardiac aneurysms occur in severe coronary disease with occlusive processes According to Sternberg,[17] 84 6 per cent of cases are due to such disease. This, perhaps, is underestimated

Since the most frequent sites of myocardial infarction are in the left ventricle, and particularly close to the apical region, the most common location of an aneurysm is in that region of the heart It occurs most often in advanced age when marked coronary disease is common. It may occasionally be observed in comparatively young individuals, as in one of the cases reported by us.[18]

Diagnosis: The diagnosis of cardiac aneurysm, especially if small, is in many cases difficult or impossible to make. The reason is that there are

no specific symptoms characteristic of the condition. There may be, however, certain findings which together with a history of a past coronary occlusion will help in the diagnosis, if the condition is borne in mind. The findings are: (1) the presence of an abnormal area of cardiac dullness, which may in some cases extend beyond the left border of the heart, (2) a forceful systolic expansion of this area may be palpated; (3) the heart sounds over this area are very weak and are out of proportion to the force-

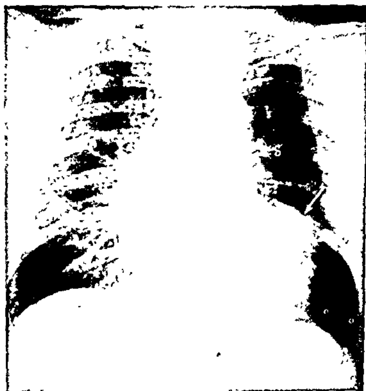


FIG. 139 — ANEURYSM ABOVE THE APICAL REGION OF THE HEART, SHOWN BY ARROW From a male, 56 years old, who sustained an attack of acute coronary occlusion with myocardial infarction of the anterior wall of the left ventricle

ful, heaving impulse; and (4) roentgenologic findings The last consist of a bulging tumorfaction at the left border of the heart, usually close to the apical region, Figure 139. This tumorfaction does not separate from the heart if the chest is rotated in different positions. Fluoroscopically, this bulging area may show an expansion instead of retraction, or may remain unaltered during systole.

Differential Diagnosis: The main conditions which may simulate a ventricular aneurysm, roentgenologically, are localized pericardial effusions,

an aneurysm of the aorta, a tumor of the mediastinum, lung or of the ventricle, or a pericardial diverticulum.

Localized pericardial effusion, shown in Figure 133, can be differentiated by the presence of pericarditis, and by the eventual disappearance of the tumorfaction.

Aneurysm of the aorta does not appear in the usual locations of aneurysm of the left ventricle, except when located in the descending thoracic portion. In such cases, fluoroscopic examination in different positions will reveal the separation of the aneurysmal mass from the heart in one or another position.

A tumor of the mediastinum or of the lung adjacent to the heart may also be differentiated from a ventricular aneurysm by a careful fluoroscopic examination A tumor of the heart itself, however, may be difficult to differentiate by such examination inasmuch as it is an integral part of the heart itself. A history of antecedent infarction and the clinical signs of a ventricular aneurysm will help arrive at the diagnosis

A pericardial diverticulum is rare. Cushing[19] quotes 39 cases from the literature, and reports a case of his own In 52.5 per cent of the cases, it occurred on the right side of the pericardium. He quotes Kienböck and Weiss who described this condition roentgenologically as an abnormal pulsating mass, rounded and sharp sides, resting against the heart He also quotes Jansson who found that this mass became long and narrow with inspiration, and more round, shorter and broader with expiration.

Myocardial Neoplasms

Primary tumors of the heart are very rare Metastatic invasion from other parts of the body are somewhat more common.

Some of the primary benign tumors encountered are myxomas, fibromas, rhabdomyomas and other rarer forms Metastatic carcinoma and sarcoma have been observed at all ages They occur more often in the auricles than ventricles, and more in the right than in the left chambers.

The diagnosis of tumors of the heart is almost impossible to make. In a series of 16 cases of metastatic tumors collected by Ritchie,[20] none were diagnosed during life It should be suspected where, in the presence of malignancy in other parts of the body, the heart develops severe disturbances in rate and rhythm.

Treatment

The treatment of the chronic degenerative processes and neoplastic infiltrations is entirely symptomatic There is nothing we can do to change the underlying pathology If cardiac decompensation occurs, treatment should be carried out as discussed in Chapter XIII.

REFERENCES

[1] Saphir, O, Wile, S A, and Reingold, I M Myocarditis in children. Am. J. Dis. Child. 67:294, 1944

[2] Gore, I, and Saphir, O Myocarditis associated with acute nasopharyngitis and acute tonsillitis Am Heart J 34 831, 1947

[3] Wendkos, M H, and Noll, J.: Myocarditis caused by epidemic parotitis Am. Heart J. 27:414, 1944

[4] Finland, M, Parker, F, Barnes, M W., and Joliffe, L. S.: Acute myocarditis in influenza A infections Am J M Sc 209:455, 1945

[5] Fiedler, A. Ueber akute interstitielle Myokoarditis Festschrift a. Feier d fünfzigjährigen Bestenens d. Stadtkrankenhauses zu Dresden-Friedrichstadt. Dresden, 1899

[6] Bailey, F R and Andersen, D H Acute interstitial myocarditis Am. Heart J 6:338, 1931

[7] Saphir, O Myocarditis in bronchiectasis Arch. Int. Med 72:775, 1943.

[8] Sigler, L H The Electrocardiogram; Its Interpretation And Clinical Application New York, Grune & Stratton 1944 Myocarditis pp 310–16, Trauma pp 323–36

[9] Smith, J J, and Furth, J Fibrosis of the endocardium and the myocardium with mural thrombosis Notes on its relation to isolated (Fiedler's) myocarditis and to beriberi heart Arch Int Med 71:602, 1943

[10] Reisinger, J A, and Blumenthal, B Myocardial degeneration with hypertrophy and failure of unknown cause Am Heart J 22 811, 1941

[11] Brown, C. E, and Evans, W D Primary massive calcification of the myocardium. Am Heart J. 19 106, 1940

[12] Diamond, M. Calcification of myocardium in premature infant. Arch. Path. 14:137, 1932.

[13] Edelstein, J M Primary, massive calcification with ossification of the myocardium Am. Heart J 31:496, 1946

[14] Roberts, J T, and Beck, C S. The effect of chronic cardiac compression on the size of the heart muscle fibers Am Heart J 22 314, 1941

[15] Sigler, L H Trauma of the heart due to non-penetrating chest injuries J.A.M.A 119: 855, 1942

[16] —— Traumatic injury of the heart Incidence of its occurrence in forty-two cases of severe accidental bodily injury Am Heart J 30:459, 1945.

[17] Sternberg, M. Das Chronische Partielle Herzaneurysma Leipzig and Vienna, F. Deuticke, 1914

[18] Sigler, L. H. and Schneider, J. J: The diagnosis of cardiac aneurysm with report of two cases. Ann Int. Med 8 1033, 1935

[19] Cushing, E H Diverticulum of pericardium Arch Int Med. 59:56, 1937.

[20] Ritchie, G Metastic tumors of the myocardium. Am J Path. 17:483, 1941.

CHAPTER XXVII

Congenital Heart Disease

THERE are a great variety of congenital defects of the heart and blood vessels, single or combined. Many of these have no clinical significance inasmuch as they do not materially interfere with the normal circulatory dynamics. Others are so serious, that the infant succumbs a few hours, or at most a few days or weeks after birth. Both of these extreme conditions will be omitted from our discussion, being but pathologic curiosities. We will also leave out from our consideration those congenital defects which, although clinically important, are very rare and must be left to the numerous existing excellent papers and monographs on the subject The "Atlas of Congenital Cardiac Disease" by Abbott[1] may be consulted for a summary of the existing material on the subject up to 1936.

In this chapter we will present only some of the more common forms of congenital heart disease Particular attention will be paid to those defects for which successful surgical correction has been employed within the past few years.

Incidence: Congenital heart disease is comparatively rare. It comprises approximately 1 to 2 per cent of all cardiac disease, and about 5 to 10 per cent of cardiac disease in childhood Its incidence varies in different parts of the world.

Classification: From a clinical viewpoint, all congenital cardiac diseases are divided into three groups: the acyanotic, the cyanose tardive, and the cyanotic This classification is based on the presence or absence of cyanosis

Acyanotic Group

In this group there is a great variety of congenital abnormalities such as, dextrocardia, pericardial defects, congenital subaortic and mitral stenosis, bicuspid aortic or pulmonic valves, supernumerary aortic or pulmonic cusps, a double mitral orifice and many others In none of the cases in this group is there any abnormal communication between the systemic and the pulmonary circulation and, therefore, no cyanosis is present.

The important abnormalities in this group, from a viewpoint of frequency, and in some cases, from a viewpoint of possible surgical relief, are coarctation of the aorta, double and right aortic arch, subaortic stenosis, hypoplasia of the aorta, and a left coronary artery originating in the pulmonary artery.

Coarctation of the Aorta

This is a comparatively common congenital defect. In routine physical examinations for the army in World War II, according to Perlman,[2] one out of every ten thousand applicants between 18 and 25 years of age presented this abnormality. The incidence is greater in other reported series, especially in younger age groups

Two types are recognized: the infantile and the adult. The *infantile type* is very serious and is usually fatal in early life because it is frequently associated with other serious malformations of the heart and great vessels. The *adult type* usually exists as a single defect and, unless very severe, is compatable with normal existence.

Pathology For a complete description of the pathology of coarctation of the aorta, the reader is referred to the paper by Edwards and co-workers[3] In brief, the defect consists of a varying degree of constriction of the descending arch of the aorta, usually in the region of the obliterated ductus arteriosus In severe cases, there may be complete obliteration of the aorta at that point As a result of this constriction, the aortic pressure above the constricted area is greatly increased, causing dilatation of the ascending and transverse portions of the arch, including the main branches originating from these portions The aorta below the constricted area is narrowed due to diminished pressure

To compensate for the diminished flow of blood though the aorta and its branches below the constriction, a more or less extensive anastomosis develops between the branches of the arch and those from the aorta below the constriction Thus, the internal mammary, intercostal and the scapular arteries become, in severe cases, markedly dilated and anastamose with the branches from the descending aorta A complete description of this anastamosis is given by Edwards and co-workers[4]

Figure 140 illustrates the usual location of coarctation of the aorta and the anastamotic arterial communications

Clinical Manifestations: The outstanding features are increased pulsation in the arteries of the upper extremities and neck and detectable pulsation of the intercostal and the interscapular arteries The pulsation of the arteries of the lower extremities is greatly diminished and may even be absent in the smaller branches There is a corresponding increase in the systolic blood pressure in the upper extremities and diminished in the lower. The diastolic pressure, according to Steel and Cohn,[5] who used a direct puncture method for its determination, is the same in the upper as in the lower extremities. This indicates that the hypertension in the upper extremities is not due to increased peripheral resistance, but to the aortic obstruction. A systolic murmur is often heard over the upper sternal

region, and more often in the left interscapular region In rare cases, there may also be heard an aortic diastolic murmur due to aortic insufficiency caused by dilatation of the aortic ring.

Subjectively, the patient may be symptom free, and the condition may be discovered accidentally Some patients may complain of dizziness, headaches or fullness in the head Others may complain of weakness and

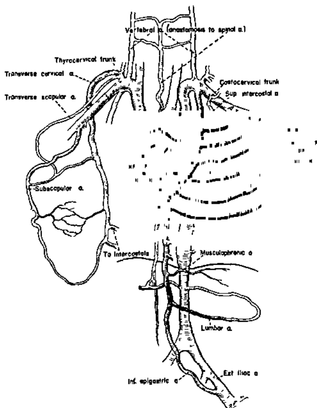


FIG 140—COARCTATION OF THE AORTA AND THE COLLATERAL CIRCULATION (After Edwards, Claggett, Drake and Christensen Proceedings Staff Meetings, Mayo Clinic July 21, 1948 Courtesy of the authors and the Mayo Foundation)

even pain in the lower extremities on exertion, the nature of which is not understood until a careful examination is made. For example, a woman, 30 years old, complained of some weakness, especially in the lower extremities, mainly on walking. Several physicians passed her on as a hypertensive and neurotic individual. Examination revealed almost absent pulsation of the vessels of the lower extremities and increased pulsation of the vessels of the upper, with associated hypertension in the latter. She had

no murmurs over the precordium, but there was a slight murmur heard in the left interscapular region, and there was some pulsation felt in the left interscapular region. Roentgenologic examination confirmed the diagnosis of coarctation of the aorta.

This case illustrates the ease with which the condition may be overlooked unless kept in mind, and unless a careful examination is made. DeBauer and Iverson[6] report two cases of coarctation who developed bacterial endarteritis at the site with aneurysm formation and embolic glomerulonephritis The coarctation was entirely overlooked during life and was found only at autopsy The hypertension was thought to be due to the glomerulonephritis.

Roentgenologic Findings: *These vary with the severity of constriction.* The aortic knob is usually greatly diminished or may be entirely absent The ascending portion of the aorta is dilated, and the left ventricle is usually enlarged. The configuration of the heart in the antero-posterior position, thus assumes a peculiar appearance, with broadening of the right base, concavity of the left base, and occasionally enlargement of the heart to the left or rounding of the apical region In the left oblique position, the descending portion of the aortic arch may not be seen Erosion of the lower margins of some of the ribs is an important confirmatory finding

Prognosis The average age at death in the reported cases of coarctation of the aorta is about 35 years In the series of 104 cases reviewed by Reifenstein and co-workers,[7] 61 per cent died before they reached 40 years of age There are a number of cases reported in the literature, however, who have lived to a ripe old age. Abbott quotes Raynod's patient, for instance, who lived to the age of 92.

Death attributable directly to the defect may be caused by rupture of the aorta, dissecting aneurysm, subacute bacterial endarteritis, congestive heart failure and cerebral hemorrhage

Surgery: The prognosis in this disease may ultimately greatly improve through surgery, especially in severe cases. The operation consists of clamping the aorta above and below the constricted area, excision of that area, and making an end-to-end anastomosis of the sectioned aorta Successful operations have been reported by Crafoord and Nylin[8] and by Blalock[9]

Double Aortic Arch

This is a rare condition of arrested development in embryonic life where the fourth bronchial arches persist and form a double aortic arch.

A full description of the various forms of this abnormality is given by Edwards.[10] In general, two main forms are recognized. The essential

features in both consist of the division of the ascending aorta into the two branches which reunite again to form the descending aorta. Two aortic arches thus exist, one in front, and the other in the back of the trachea and esophagus, forming a vascular ring around these structures. This is illustrated in Figure 141

Some of the cases presenting this condition are asymptomatic, and may go through life unrecognized In the more severe cases, a metallic cough, noisy breathing and dysphagia, especially of solid foods may occur. There is also a tendency for frequently recurring bronchitis These symptoms occurring in youth should make one suspicious of the presence of this condition

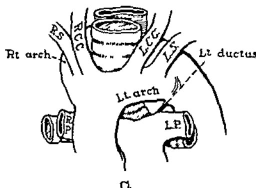


FIG. 141—DOUBLE AORTIC ARCH (After Edwards, Medical Clinics, North America July 1948 Courtesy of the author and W B Saunders Company)

Roentgenologic examination with a barium filled esophagus will reveal compression of the esophagus and trachea in the region of the aortic arch

Surgery In severe cases, operative section of one of the arches is necessary to relieve the condition This was first successfully performed by Gross[11]

Subaortic Stenosis

This is a rare congenital condition characterized by a raised, firm, fibrous ring below the base of the aortic valve, but not involving the valve itself Young[12] found this condition in ten instances among 18,000 selected soldiers He believes that its general incidence is greater.

The condition is usually asymptomatic, although some of the cases present general underdevelopment. It may become the seat of subacute bacterial endocarditis, or in later life, it may predispose to left heart failure

In uncomplicated cases, the condition may be recognized by a harsh murmur and thrill similar to those observed in aortic stenosis. The murmur

and thrill are transmitted to the vessels of the neck. Unlike those of aortic stenosis, however, the murmur and thrill in this condition diminish in intensity in the recumbent position and during inspiration, and are usually followed by a normal aortic second sound. Also, the blood pressure may be normal. Left ventricular enlargement is usually present. The absence of a history of rheumatic fever or arteriosclerosis, and the presence of a murmur from early infancy are further aids in the diagnosis of this condition

Left Coronary Artery Originating from the Pulmonary Artery

This condition is very rare. In a review of the literature, Kannitz[13] found only 25 cases in which the condition occurred as a single anomaly, and he added 2 cases of his own

Most cases succumb in infancy or early childhood, as the condition is incompatible with normal existence A chronic anoxia of the left ventricle occurs in this condition, because the left coronary artery derives venous instead of arterial blood from the pulmonary artery, and also, because the intrapulmonic arterial pressure is lower than the intra-aortic pressure, which reduces the force of the flow of blood in the left coronary artery

The pathologic findings consist of hypertrophy and dilatation of the left ventricle with necrosis and fibrosis of the myocardium and dilated sinuses, as well as degenerative changes of the endocardium.

The clinical features consist of paroxysmal cardiac pain, pallor, cyanosis, dyspnea, marked cardiac enlargement, and later, pulmonary edema These manifestations occurring in childhood with no evidence of rheumatic valvular disease or other conditions leading to left heart enlargement should lead one to suspect this condition Eidlow and MacKenzie[14] reported a case that they diagnosed correctly during life and proved by autopsy

CYANOSE TARDIVE GROUP

In this group of congenital cardiac diseases are placed those cases presenting some communication between the right and left chambers of the heart, or between the aorta and pulmonary artery Because the pressure is normally greater in the left chambers of the heart and aorta than in the right chambers and pulmonary artery, the abnormal flow will occur from the arterial to the venous side of the circulation, and no cyanosis will be present When some unusual situation arises which suddenly increases the pressure in the right ventricle and pulmonary artery, there will be a reversal of the flow of blood from the venous to the arterial side and cyanosis will occur

The conditions under this heading include patent ductus arteriosus, and patent interauricular and interventricular septa

Patent Ductus Arteriosus

This congenital defect consists of the persistence of patency of the duct which connects the aorta and pulmonary artery in the intrauterine life of the fetus. Normally, this duct closes, according to Christ, as quoted by Gross[15] in 95 per cent of cases by the end of twelve weeks after birth, and in about 99 per cent of cases by the end of one year. In rare cases, spontaneous closure may occur later in childhood or even in adulthood, as in the two cases observed by Shapiro and Keys.[16] However, in most of the cases where it does not close within the first few years of life, it remains permanently patent.

Incidence. The exact incidence of occurrence of this abnormality is not definitely known. It is considered to be the third most frequent form of the congenital cardiovascular defects It is seen with the greatest frequency in the younger age groups Thus, among 82 cases quoted from the literature by Gilchrist,[17] 33 were children less than 10 years old, 24 were between 11 and 20 years, 10 between 21 and 30 years, 12 between 31 and 50 years, and only 3 between 51 and 60 years of age In other words, about 70 per cent of cases were below 20 years, and 82 per cent below 30 years of age The reasons for the scanty number of reported cases in adults, according to Gilchrist, are that many die in youth, that spontaneous closure may occur in later childhood, and that clinicians and pathologists fail to look for this defect

Disturbances in Hemodynamics As a result of the abnormal communication between the aorta and pulmonary artery, and because of the normally greater intra-aortic than intrapulmonic pressure, there is a shunting of blood from the aorta into the pulmonary artery According to Eppinger and co-workers,[18] the volume of blood so shunted is about 45 per cent to 75 per cent of that leaving the left ventricle This extra volume of blood loaded in the pulmonary artery in addition to that entering this artery from the right ventricle greatly distends the pulmonary vascular tree, and sends forth a relatively greater volume of blood into the left auricle and ventricle than the right auricle and ventricle receive during the same cardiac cycle According to Eppinger and co-workers,[18] the left ventricle has to pump two to four times as much blood as the right ventricle in these cases. Because of the increased volume of blood entering the left auricle, the mitral valve may be relatively too narrow to allow complete emptying of the left auricular contents during each cycle, so that the left auricle may gradually become enlarged. The circulatory changes in this condition are illustrated in Figure 142.

Inasmuch as the flow of blood through the patent ductus normally occurs from the aorta which carries oxygenated blood to the pulmonary artery, the

oxygen saturation of the blood in the latter is greater than normal. Also, the oxygen saturation of the systemic arterial blood is not affected. Hence, no cyanosis is present in these cases. If, however, the pressure in the pulmonary artery becomes greater than in the aorta due to extensive pulmonary disease, or to a rise in intrathoracic pressure caused by severe cough, by crying or other reason, there will be a reversal of flow in the direction from the pulmonary artery into the aorta. Under such circumstances, some degree of transient cyanosis may develop, spoken of as "cyanose tardive."

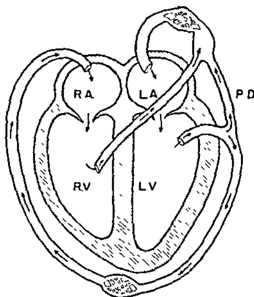


FIG 142.—DIAGRAM ILLUSTRATING THE CIRCULATORY ALTERATIONS IN PATENT DUCTUS ARTERIOSUS Part of the blood leaving the left ventricle, L. V, through the aorta is diverted through the patent ductus, P D, to the pulmonary artery and to the lungs Arrows indicate direction of blood flow to the heart and from the heart R A, right auricle, R V, right ventricle; L A, left auricle, and L V, left ventricle

This is also true if the disease occurs in stocky, short-chested individuals with high diaphragms and poor excursions. In such cases, there may be frequent fluctuations in the intrapulmonic arterial pressure resulting in a

low

the

systemic arteries, as in other arteriovenous fistulae. The wider the patency the lower the diastolic pressure If the caliber of the ductus is very large, peripheral vascular signs similar to those observed in high grade aortic insufficiency may develop.

Clinical Manifestations: The subjective manifestations depend upon the degree of patency. In mild cases, there may be no disturbance and the patient may not be aware of the existence of any defect until told about it The author has observed several patients with unmistakable evidence of this abnormality who have been working at heavy manual labor without any ill effects. He has also had some female patients who have gone through one or more pregnancies with no untoward effects.

If the defect is marked, however, the patient does not thrive well. He may present moderate pallor, undernourishment, retardation in mental and physical development and he may not be able to carry on a normal amount of physical activity. There may be evidence of cardiac embarrassment under any strain and even frank congestive failure may develop.

On percussion, the heart may be found to be more or less enlarged, and there is a varying degree of widening in the area of dullness in the second and third left interspaces.

Auscultation reveals the characteristic murmur originally described by Gibson [19] According to Abbott, the character of the murmur varies with the length of the canal and the shape of its orifice. The murmur is often described as a "machinery" or "train in tunnel" type. It is usually rough, humming or gurgling It begins after the onset of the first heart sound and continues through the rest of systole and part of diastole, frequently enveloping the second sound. It is usually heard with maximum intensity at the pulmonic area and extends to the first and third interspaces. If loud, it may extend over a much wider area, and may be heard also over the back of the chest. In Abbott's 92 cases, 30 per cent showed only a systolic mur- [illegible]

or even at the apex. In infants and very young children, the systolic murmur is most frequent.

Levine and Geremia[20] observed 4 cases who also showed a mid-diastolic murmur resembling that heard in mitral stenosis. In about one-third of cases the murmur is accompanied by a thrill felt over the area where the murmur is heard In rare cases there may be no murmur The pulmonic second sound may be accentuated or reduplicated

Roentgenologic Findings: These are more or less characteristic. There is a varying degree of bulging of the pulmonic conus and pulmonary arterial radicals. The latter is evinced by an increase in the hilar and vascular markings. These are shown in Figure 143 There may also be some enlargement of the left auricle and left ventricle In occasional cases, there may be slight enlargement of the right ventricle. Fluoroscopically, we may find excessive pulsation of the pulmonary arterial

branches, spoken of as "hilar dance," and increased pulsation of the left ventricle.

Differential Diagnosis The most important diagnostic criteria of this disease are the prominence of the pulmonic conus, seen roentgenologically, and the characteristic murmur The former may occur in other congenital or acquired conditions, such as interauricular septal defects, Eisenmenger

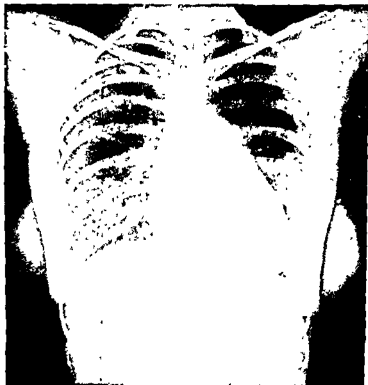


FIG 143—TELEOROENTGENOGRAM IN PATENT DUCTUS ARTERIOSIS Marked bulging o pulmonic conus, enlargement of the heart downwards and to the left, and prominence of hilar markings From a female, 28 years old

complex, pulmonary insufficiency due to absence of cusps, mitral stenosis, chronic pulmonary disease, and other conditions producing pulmonary arterial hypertension, as discussed in Chapter XVIII. The differential diagnosis is based on clinical and other x-ray findings in these various conditions, as described under the respective diseases. In cases where the characteristic murmurs in this disease are present, the diagnosis can not be mistaken. When the murmur, however, is systolic in time, it may resemble that of pulmonary stenosis. In the latter, however, cyanosis and

clubbing of fingers and toes are almost the rule, and the second pulmonic sound is usually absent or weak A fall in diastolic pressure after exercise which occurs in patent ductus arteriosus is another diagnostic criterion. Where the patency is large, a high pulse pressure, capillary pulsation, a pistol-shot sound heard over the peripheral arteries coupled with the configuration of the heart and the murmur help to confirm the diagnosis.

Prognosis: As said before, the great majority of cases having this disease die before they reach middle adult life The average longevity of Abbott's series of 92 cases was 24 years. The cause of death was congestive failure in 43 per cent and subacute bacterial endoarteritis in 30 per cent of cases. In the cases collected from the literature by Shapiro and Keys, 80 per cent succumbed to the lesion, an equal number dying from congestive failure as from subactute bacterial endoarteritis.

Surgical Treatment The successful ligation of the patent ductus first performed by Gross and Hubbard,[21] and the postoperative recovery from subacute bacterial endoarteritis superimposed upon patent ductus arteriosus, reported by Touroff and Vesell,[22] show promise of great improvement in the ultimate prognosis of this disease Many cases have since been operated on by other surgeons with great success Shapiro and Johnson[23] have collected 643 cases who were operated on by 46 different surgeons The diagnosis was confirmed in 626 of these cases at operation. Of these 626 cases, 525 were noninfected and 101 had subacute bacterial endoarteritis superimposed. The over-all operative mortality rate was only 4 9 per cent. In 8.7 per cent of cases recanalization occurred This will undoubtedly be prevented in the future by employing the method of complete surgical division of the ductus wherever possible, as recommended by Gross [24]

At the present writing, the operation is recommended mainly in those cases that do not thrive well, and who show mental or physical retardation, or suffer from cardiac embarrassment or from intermittent decompensation. It is also advised in cases complicated with subacute bacterial endarteritis. Other cases should be carefully considered from a viewpoint of possible future development of these disturbances

Interauricular Septal Defect

This is the most common form of congenital heart disease In the past, the vast majority of cases were undiagnosed during life. This was clearly shown by Roesler[25] who collected 62 autopsy cases from the literature and found that only 1 had been diagnosed during life, and in 4 others it had only been suspected

Within the past decade, however, the diagnosis of this condition has been

made more frequently. Thus, Bedford and co-workers[28] in a comprehensive review of the subject report 53 cases of their own in which the diagnosis was made, and in 10 of these the diagnosis was proved by autopsy.

Pathology: From a clinical viewpoint, only septal defects of about 1 centimeter or more in diameter are of significance. Smaller defects, which frequently occur in normal individuals in the foramen ovale, are nonproductive of symptoms and signs. In rare cases, however, even these may increase an existing cyanosis in congestive heart failure when the right



FIG 144—MARKED PATENCY OF THE INTERAURICULAR SEPTUM There is an associated shortening and thickening of the chordae and the mitral leaflets are moderately interadherent, indicating the coexistence of mitral stenosis—Lutenbacher's disease. (From Edwards, Post Graduate Medicine, May 1948 Courtesy of the author and the publishers)

auricular pressure becomes greater than the left. They may also serve as a means of paradoxical embolization.

Auricular septal defects are frequently associated with other congenital abnormalities of the heart, such as patent ductus arteriosis, ventricular septal defects, and so on It is also often associated with mitral valvular disease, especially mitral stenosis The latter condition is often spoken of as Lutembacher's disease It is illustrated in Figure 144 In Roesler's series as well as in that of Burnett and White,[24] 53 8 per cent of cases had associated mitral stenosis. In 7 to 25 per cent of cases, however, an auricular septal defect exists as a single lesion, according to Bedford and coworkers.

Because of the normally greater pressure in the left than in the right auricle, the flow of blood through an auricular septal defect occurs from the left to right This is evidenced by the greater oxygen content of the blood in the right heart than in normal cases, as was shown by catheterization of the heart chamber by Brannon and co-workers.[28] This results in greater filling of the right auricle which receives blood from both the venae cavae and the left heart The right auricle, therefore, dilates and eventually undergoes hypertrophy. The increased filling of the right auricle results in increased filling, also, of the right ventricle and pulmonary artery with their consequent enlargement. In occasional cases, some degree of tri-

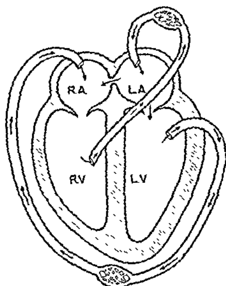


FIG 145—DIAGRAM ILLUSTRATING THE CIRCULATORY CHANGES IN PATENT INTERAURICULAR SEPTUM

cuspid insufficiency occurs due to dilatation of the auriculo-ventricular orifice in the right heart caused by distention In late stages, right heart failure ensues The circulatory changes in this condition are illustrated in Figure 145

Subjective Manifestations This defect may exist for many years without any symptoms For this reason the condition is often overlooked. The earliest symptom is exertional dyspnea. This is due to pulmonary vascular engorgement reducing the alveolar spaces in the lungs. In later stages, symptoms and signs of right heart failure develop. Cyanosis and other signs of right heart failure then become important findings, as discussed in Chapter XIII.

Physical Findings. These, like the subjective manifestations, are not characteristic, except for more or less right auricular, right ventricular and pulmonary artery enlargement These in the absence of mitral stenosis, and without definite signs of patent ductus arteriosus, pulmonary artery atresia or sclerosis should suggest the presence of the condition. In the presence of mitral stenosis, it is at times, difficult to diagnose a co-existing patent interauricular septum. In some cases, however, the mitral diastolic rumble of mitral stenosis, may be absent, inasmuch as the left intra-auricular pressure is low due to the escape of blood from the left into the right auricle.

There are no characteristic murmurs in patent interauricular septum by which the condition may be recognized, although some murmurs may be heard *in different cases and at different times, which by inference, may help* in our diagnosis. Thus, a low intensity systolic murmur may be heard in the third or fourth left interspace close to the sternum due, perhaps, to pulmonary artery dilatation. This is followed by an accentuated pulmonic second sound In occasional cases, a soft diastolic murmur is heard over the pulmonic area, due to dilatation of the pulmonic valve. Bedford and co-workers found this murmur in ten of their cases Occasionally, a systolic murmur may also be heard at the apex, the lower sternal region, or over the xyphoid area due to some tricuspid insufficiency. The patent interauricular septum itself, apparently produces no murmur

Roentgenologic Findings: In the antero-posterior view, the heart is enlarged to the right and left, and assumes a globular shape The left border is convex due to right ventricular enlargement which extends to the left, displacing the left ventricle backwards There is marked bulging of the pulmonic conus and artery, and there is some dilatation of the right pulmonary branch, *which assumes a comma-shaped appearance The right border is* usually markedly convex and there may be an elongation of the right auricular curve. Figure 146 is an example of an advanced case. Fluoroscopically, there is noted an increased pulsation of the pulmonary artery and the right branch. The latter is often spoken of as the "hilar dance," as in patent ductus arteriosus. The pulsation in interauricular septal defect is usually greater, however. In the right oblique position, there is an increased width of the upper cardiac silhouette due to the dilated pulmonary artery, and the posterior border in the region of the left auricle is straightened A barium esophagram shows no compression of the esophagus in the region of the left auricle, a diminished compression in the aortic region, and a greater compression in the region of the pulmonary artery. In the left oblique position, the prominent right ventricle approaches the sternal border of the heart.

The electrocardiogram usually shows more or less right axis deviation with

or without notching of the QRS complex. The P wave is usually larger than normal.

Differential Diagnosis: The x-ray configuration of the heart in this disease may resemble that of pure mitral stenosis, patent ductus arteriosis, cor pulmonale, or a few rarer conditions. Mitral stenosis may be differentiated by the characteristic rumble, enlarged left auricle, and in many cases there is a history of rheumatic fever Patent ductus arteriosis is



FIG 146—FROM A MALE, 48 YEARS OLD, WITH MARKED DEGREE OF INTERAURICULAR SEPTAL DEFECT

differentiated in most cases, by the characteristic murmur, no right auricular and very little, if any, right ventricular enlargement. The left ventricle is usually enlarged Cor pulmonale can be recognized by the cyanosis and the presence of pulmonary disease.

Prognosis: The interesting feature of this disease is the relative infrequency of serious complications and of symptoms. The condition also has a fair longevity. Over 50 per cent of reported cases lived beyond 40 years of age, and the average longevity is about 37 years. In Roesler's series, the youngest age at death was 11 months, and the oldest, 75 years.

Subacute bacterial endocarditis is extremely rare, and an occasional death from paradoxical embolization has been reported. The usual mode of death is congestive right heart failure and occasionally bronchopneumonia

Interventricular Septal Defect

This may occur as an isolated lesion, although in many cases other defects coexist The usual location of the patency is in the membranous portion of the interventricular septum, as shown in Figure 147. In rarer cases, it occurs in other parts. In uncomplicated cases, the condition is

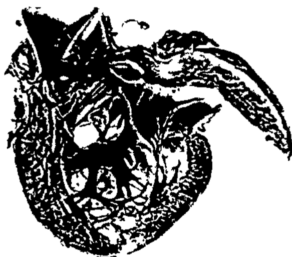


FIG 147—INTERVENTRICULAR SEPTAL DEFECT IN THE MEMBRANOUS PORTION OF THE VENTRICULAR SEPTUM Part of the defect contains a segment of the septal leaflet of the tricuspid valve and its chordae tendineae The defect is viewed from the interior of the left ventricle (From Edwards, Postgraduate Medicine, May 1948 Courtesy of the author and publishers)

asymptomatic. It is recognized by a harsh, holosystolic murmur with maximum intensity in the third or fourth left interspaces and wide area of transmission. In some cases there may also be a systolic thrill in the same location.

Inasmuch as the flow of blood through the defect is normally in the direction from the left ventricle to the right, due to higher interventricular

ht

ıw

ht

ventricle usually develops and accentuation of the pulmonic second sound

is observed. In some cases, a variable degree of auriculo-ventricular block is observed.

The average span of life in these cases is about 14 years Death may be due to congestive heart failure, bronchopneumonia, subacute bacterial endocarditis, or other causes In some cases, death may be sudden and unexplainable.

The Cyanotic Group

There is great variety of congenital defects which produce permanent cyanosis. In general, they are divided into two classes. In one, the condition is caused by congenital stenosis of the valves of the right heart without any shunts. In the other, shunting exists between the systemic and pulmonic circulations. One of the most important conditions of the former is pulmonary stenosis and of the latter, the tetralogy of Fallot.

Pulmonary Stenosis

We shall include, here, only the extremely rare case of pulmonary stenosis without any complicating venous-arterial shunts.

This group of cases may be divided in two subgroups In one, the stenosis does not affect the valve itself, but occurs some distance below the valve, forming a small chamber through which the venous blood must pass In the floor of this small chamber there is a small stenosed opening communicating with the main right ventricular cavity This condition is due to congenital maldevelopment. In the other group, there is actual stenosis of the pulmonary valve, believed to be caused in most cases, by inflammatory changes of the endocardium in later intrauterine life of the fetus, after the separation of the chambers has been completed In rare cases the tricuspid valve may also be affected.

The cyanosis in this condition is not marked, and develops later in life. Clubbing of the fingers and toes, likewise, develops gradually Both the cyanosis and clubbing may, in some cases, become quite marked as time progresses A harsh systolic murmur and marked thrill are present at the pulmonic area which may be heard with much less intensity in the back of the chest, close to the left scapular region The murmur is not transmitted to the vessels of the neck, unlike that of aortic stenosis. The right ventricle is greatly enlarged and the electrocardiogram shows marked right ventricular preponderance Figure 129 shows the location and transmission of the murmur and the associated cardiac enlargement.

Tetralogy of Fallot

This form of congenital maldevelopment consists of pulmonary stenosis, interventricular septal defect, dextraposition of the aorta, the opening of which overrides the septal defect, and right ventricular hypertrophy, as

shown in Figure 148. The pulmonary stenosis in these cases usually includes narrowing and hypoplasia of the entire pulmonary arterial tree and the pulmonary valve is usually bicuspid.

Disturbances in Hemodynamics Because of the interference with the free expulsion of blood from the right ventricle into the pulmonary artery



Fig 148—Tetralogy of Fallot, from a Boy 7 Years Old The interior of the right ventricle is exposed, showing a large interventricular septal defect, D, in the membranous portion The aorta, A, is wide and straddles the septal defect, thus communicating in part with the right ventricle The pulmonary artery, P, is narrow, and there is a narrow subpulmonary "third ventricle," S The wall of the right ventricle is thick (From Edwards, Bulbulian and Rogers, Proceedings Staff Meetings, Mayo Clinic April 30, 1947 Courtesy of the authors and the Mayo Foundation)

due to the stenosis, there is increased pressure in the right ventricle. The [illegible]

goes marked compensatory hypertrophy. The circulatory changes are illustrated in Figure 149

The shunting of much of the venous blood into the aorta and the systemic arteries results in marked cyanosis. This is intensified by diminished oxygenation of the blood due to pulmonary atresia, as well as by the prolonged capillary dilatation at the periphery There is marked compensatory polycythemia, varying between seven and twelve million cells per cubic millimeter, which further accentuates the cyanosis.

Clinical Manifestations: This congenital condition is characterized by most intense cyanosis and enormous clubbing of the fingers and toes. In many of the cases the cyanosis and clubbing develops with greatest inten-

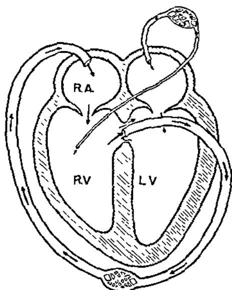


FIG 149 —DIAGRAM ILLUSTRATING THE CIRCULATORY CHANGES IN THE TETRALOGY OF FALLOT.

sity one year or longer after birth, when a coexisting patent ductus arteriosus, which may be present, closes The heart is markedly enlarged with elongation and rounding of the right border and some concavity of the upper left border, producing the x-ray appearance of the typical so-called "coeur-en-sabot" or shoe-shaped heart There is usually a long, rough systolic murmur heard with its maximum intensity at the second left interspace, associated with a thrill. The electrocardiogram shows marked right ventricular preponderance and a high P wave

Prognosis. In Abbott's series of 83 cases of tetralogy of Fallot, the average longevity was 12¾ years, the oldest age being about 25 years. White and Sprague[23] reported a case of an accomplished musician suffering

from this disease who lived to an unusually long age of about 60 The usual cause of death in all cases is heart failure, except for thos die from intercurrent disease

Surgery The recent successful operations in cases with pulmonary sis and atresia with or without other defects, reported by Blaloc Taussig,[30] promise to improve the prognosis of this disease The ope consists of the establishment of an artificial "ductus arteriosus" by tamosing one of the main arterial branches of the aortic arch with a b of the pulmonary artery Shunting of the blood from the aorta to th monary tree is thus accomplished, allowing oxygenation of a greater v of blood in the lungs The operation is contraindicated, of course, cases where the pulmonary conus is prominent and there is evident j tion of the hilar region of the lung.

Eisenmenger Complex

This rare congenital defect is similar to tetralogy of Fallot excej the absence of pulmonary stenosis or hypoplasia. Cyanosis and clu of the fingers are not marked and appear late in the disease. In some there may not be any clubbing at all There is a systolic murmur h characteristic of ventricular septal defect, over the third and fourt interspaces, transmitted to the back, but not to the vessels of the ne

THE EVALUATION OF SURGERY IN CONGENITAL HEART DISEAS

The interesting pioneer surgical work in congenital heart disease, init by Gross, Hubbard, Blalock, Taussig, Crooford, Nylin and other wo mentioned in this chapter hold out promise for future relief of suff and for prevention of early death from congenital malformations of the and great vessels To date, thousands of cases have already been suc fully operated on, relieving the patient of suffering and prolonging hi The ultimate outcome of these operations, however, will have to be c mined by future observations Permanent benefits may be expect successful operations on patent ductus arteriosus, coarctation of the a and in the relief of vascular constrictive rings In cases of pulmo stenosis, however, although great immediate improvement is noted most that is accomplished is the establishment of an artificial comn cation between the systemic and pulmonic circulations, a condition w we are trying to overcome in cases of patent ductus arteriosus. Th timate outcome in these cases, therefore, is expected to be poor How if we can improve the physical and mental states of the infants and chil suffering from this disease and prolong their lives, which heretofore very short, much will be accomplished

REFERENCES

[1] Abbott, Maude E · Atlas of Congenital Cardiac Disease New York, American Heart Association, 1936.
[2] Perlman, L· Coarctation of the aorta Clinical and roentgenologic analysis of thirteen cases Am Heart J. 28 24, 1944
[3] Edwards, J. E, Christensen, N A, Claggett, O T, and McDonald, J R Pathologic considerations in coarctation of the aorta Proc Staff Meet Mayo Clin 23 324, 1948
[4] ——, Claggett, T. O, Drake, R L, and Christensen, N A The collateral circulation in coarctation of the aorta Proc Staff Meet Mayo Clin 23 333, 1948
[5] Steel, J. M, and Cohn, A E Nature of hypertension in coarctation of the aorta J Clin Investigation 17 514, 1938
[6] DeBauer, D, and Iverson, L Coarctation of the aorta—Report of two cases Am Heart J 30 30, 1945
[7] Reifenstein, G H, Levine, S A, and Gross, R E Coarctation of the aorta A review of 104 autopsied cases of the "adult type" 2 years of age or older Am Heart J 33 146, 1947
[8] Crafoord, C, and Nylin, G Congenital coarctation of aorta and its surgical treatment J. Thorac. Surg 14 347, 1945
[9] Blalock, A Physiopathology and surgical treatment of congenital cardiovascular defects Bull N Y Acad Med 22 57, 1946
[10] Edwards, J E Anomalies of the derivatives of the aortic arch system Med Clin North America Mayo Clinic Number July 1948
[11] Gross, R E Surgical treatment for dysphagia lusoria Ann Surg 124 532, 1946
[12] Young, D Congenital subaortic stenosis Am Heart J 28.440, 1944
[13] Kaunitz, P E Origin of left coronary artery from pulmonary artery Am Heart J 33 182, 1947
[14] Edlow, S, and MacKenzie, E R Anomalous origin of the left coronary artery from the pulmonary artery Report of a case diagnosed clinically and confirmed by autopsy Am Heart J 32 243, 1946
[15] Gross, R E *Experiences with surgical treatment in ten cases of patent ductus arteriosus* J A M A 115 1257, 1940
[16] Shapiro, M J, and Keys, A The prognosis of untreated patent ductus arteriosus and the results of surgical intervention Am J M Sc 206 174, 1943
[17] Gilchrist, A R Patent ductus arteriosus and its surgical treatment Brit Heart J 7 1, 1945.
[18] Eppinger, E C, Burwell, C S, and Gross, R E Effects of patent ductus arteriosus on circulation J Clin Investigation 20 127, 1941
[19] Gibson, G A Diseases of the Heart and Aorta Edinburgh, Young J Pentland, 1898.
[20] Levine, S A, and Geremia, A E Clinical features of patent ductus arteriosus with special reference to cardiac murmurs Am J M Sc 313 285, 1947
[21] Gross, R E, and Hubbard, J P Surgical ligation of a patent ductus arteriosus Report of first successful case J A M A 112·729, 1939
[22] Touroff, A S W, and Vesell, H Subacute streptococcus viridans endarteritis complicating patent ductus arteriosus J A M A 115 1270, 1940
[23] Shapiro, M J, and Johnson, E Results of surgery in patent ductus arteriosus Am Heart J 33·725, 1947
[24] Gross, R E Complete surgical division of the patent ductus arteriosus Surg, Gynec & Obst 78 36, 1944
[25] Roesler, H Interatrial septal defect Arch Int Med 54 339, 1934
[26] Bedford, D E, Papp, C, and Parkinson, J Atrial septal defect Brit Heart J 3 37, 1941.

[27] Burrett, J B, and White, P D Large interauricular septal defect with particular reference to diagnosis and longevity Am J M Sc 209 355, 1945
[28] Brannon, E S, Weens, H S, and Warren, J V Atrial septal defect Study of hemodynamics by the technic of right heart catheterization Am J M Sc 210 480, 1945
[29] White, P D, and Sprague, H B "The tetralogy of Fallot" Report of a case of a noted musician who lived to his sixtieth year J A M A 92 787, 1929
[30] Blalock, A, and Taussig, H B The surgical treatment of malformations of the heart J A M A 128 189, 1945

CHAPTER XXVIII

Cardiovascular Abnormalities in the Endocrinopathies and in Avitaminosis

THE CARDIOVASCULAR system, like other parts of the body, may be profoundly affected by certain endocrine disturbances and vitamin deficiency. The best known of these are dysfunction of the thyroid, adrenals and pancreas, and deficiency of vitamin B_1

THYROID DYSFUNCTION

Disease of the thyroid gland may result in hyper- and hypofunction of that gland The former is spoken of as hyperthyroidism and the latter as hypothyroidism In occasional cases, extreme enlargement of the gland without functional disturbances may result in local compression symptoms

Hyperthyroidism

This condition is often spoken of as thyrotoxicosis The latter term is perhaps more descriptive than the term hyperthyroidism, inasmuch as some manifestations of the disease can not be ascribed merely to an excessive thyroid secretion, but to some as yet unknown *toxic* material found in such secretion

Etiology

The underlying cause or causes are not fully established Heredity appears to play a great part The disease frequently occurs in more than one member of the same family It is more frequent in the female sex, the ratio being about 4 to 1 The usual age of its occurrence is between 35 and 45 years, but it has been observed in childhood and in senility The oldest case under the author's observation was a female, 72 years old It usually follows extreme nervous shock, strain or emotional disturbance It is more frequent in some regions of the world than in others Thus, in the United States, Coffen[1] found an incidence of 6 1 per cent of thyrotoxicosis among 3,488 cardiac cases in Oregon, while in the New England states, White and Jones[2] found the incidence to be less than 3 per cent

Physiologic Mechanism

The increased and abnormal thyroid secretion may be due to structural or adenomatous changes in the thyroid gland, to excessive production

of the thyroid stimulating hormone of the anterior pituitary body, or to an excessive stimulating effect of the autonomic nervous system on the thyroid or on the pituitary gland

The manner in which the heart and the vascular system are affected by the thyrotoxic state is not as yet entirely clear. It appears to be mainly the result of an increase in the metabolic activity of all the body cells, induced by the thyroid toxin This increased metabolic activity results in a greater amount of heat production and heat dissipation, and calls for an increased oxygen consumption and, therefore, a greater demand on the part of the tissues for greater blood supply. The oxygen consumption has been found to increase in this disease as much as 80 per cent above normal, in some cases, and in occasional instances, even higher

The demand for increased blood supply is accomplished by an acceleration of the heart rate, an increased force of cardiac contraction and an increase in its minute volume output as shown by Burwell and co-workers[3] The increased minute volume output is due mainly to an increase in the *number of beats per minute* *The cardiac output, according to Boothby* and Rynearson,[4] is proportionately greater than the oxygen consumption, as shown by a subnormal arteriovenous oxygen difference. In this respect there is a difference in the cardiovascular response in this disease from that of increased activity due to physical strain in normal individuals In the latter, the cardiac response corresponds to the increased oxygen consumption during such activity. The blood flow is greatly accelerated, as shown by Blumgart,[5] and the blood volume is increased, as shown by Thompson[6]

These factors are associated with widespread arteriolo-capillary dilatation promoting a greater flow of blood to the hyperactive tissues as well as to the surface of the body The arteriolo-capillary dilatation results in some reduction in the diastolic blood pressure The systolic pressure may remain normal or may be elevated The capillary dilatation on the surface of the body and the increased activity of the sweat glands promote greater dissipation of heat. This is Nature's method of overcoming the increased heat production caused by a heightened metabolism.

Although the cardiac manifestations appear to be mainly a response to constitutional demands for greater blood supply to the body, the thyrotoxin appears to have some direct effect on the heart itself, as has been shown by Lewis and McEachern[7] They observed that isolated hearts fed with thyroid substance showed a more rapid rate than normal preparations under similar conditions The occurrence of various cardiac arrhythmias in this disease, particularly auricular fibrillation, also suggests a possible direct toxic effect on the heart. There is a possibility, however, that the arrhythmias are partly due to vago-sympathetic disturbances.

They may also be due to some relative vitamin deficiency, which may develop in this disease as a result of increased metabolism, as suggested by Means and Richardson.[8]

Pathology

Thyrotoxicosis produces no definite structural changes in the heart and vascular tree. In occasional chronic cases, some cardiac hypertrophy has been found In the majority of such cases, however, there are other coexisting conditions such as coronary sclerosis, hypertension and valvular disease which would account for such hypertrophy. Prolonged auricular fibrillation, often observed, which leads in some cases to congestive failure, may also be the cause of cardiac enlargement. Among 27 fatal cases, Friedberg and Sohval[9] observed cardiac hypertrophy in only 14. Twelve of these had severe coronary sclerosis, hypertension and established auricular fibrillation In the remaining two, the hypertrophy was slight This appears to be the experience of other authors, also, although some have observed hypertrophy in a greater proportion of cases Thus McEachem and Rake[10] found hypertrophy in 16 of 27 autopsied cases Experimentally, Simonds and Brandes[11] produced cardiac hypertrophy in dogs by feeding them thyroid extract

Clinical Manifestations

These depend upon the disturbed physiology resulting from the toxic state The manifestations are in proportion to the degree of toxicity and to the sensitivity of the patient.

As a result of the increased metabolism, there is progressive loss of weight in many individuals with a corresponding increase in appetite. Sweating may be very marked and is accompanied by thirst to overcome the loss of water from the body There is marked increase in nervous irritability and occasionally considerable emotional instability The author has observed several cases with definite psychosis. Frequently, there are marked gastro-intestinal disturbances with diarrhea, resulting from disturbances in the vegetative nervous system. Tremors of the muscles often occur, best demonstrated by the outstretched hands. Exophthalmus occurs in some cases, and in others there may merely be some widening of the palpebral fissures, producing a more or less characteristic stare. The skin is warm and often moist, and flushing of the face, neck and upper chest is frequently noted. Due to capillary hypersensitivity, dermographia is a frequent manifestation

In most cases, the thyroid gland shows a varying degree of enlargement which may be diffuse of localized Its consistency varies in different cases. It may be soft, cystic or hard and nodular. In occasional cases, no definite

enlargement can be demonstrated, and in some cases the thyroid may be substernally placed so that the presence of some enlargement may, at times, be difficult to demonstrate, except perhaps, by x-ray.

The heart disturbances are often the outstanding features of the disease. Rapid or irregular palpitation is almost an invariable complaint and dyspnea is often a prominent symptom. In some cases, precordial discomfort, or even the anginal syndrome may develop in the course of time. This is true, especially in individuals of the arteriosclerotic age. Transient recurring dizziness is often complained of. In the later stages, congestive failure may occur if the condition is unrelieved. This is true, particularly, if other coexistent heart disease is present. In a review of 409 cases of thyrotoxicosis, Likoff and Levine[12] found that of 331 uncomplicated cases, only 21, or 6.3 per cent developed congestive failure, while in 78 cases complicated by other heart disease, 39, or 50 per cent developed such failure

The physical findings reveal a marked increase in the precordial heave, extending far beyond the normal apex beat This often gives the impression of the presence of cardiac hypertrophy, although careful percussion and roentgenologic study usually fail to reveal any enlargement of the heart in uncomplicated cases. The heart sounds are markedly accentuated, and a systolic murmur is often heard at the apex and along the left sternal border. The rate is usually greatly accelerated, the average being between 100 and 120 beats per minute. At times it may reach 150 or more, but in occasional cases it may be as low as 80 or even less. Auricular fibrillation is a frequent occurrence, being present in about 20 per cent of cases Early, it may be a transient but frequently recurring manifestation, but later it may become permanent It is often precipitated by any low grade febrile disease, excitement or strain Transient, recurring auricular fibrillation in the absence of organic heart disease, or even in the presence of valvular pathology should always arouse the suspicion of the possible presence of thyrotoxicosis In rare cases, auricular flutter or paroxysmal tachycardia may occur

The blood pressure in uncomplicated cases usually shows a normal, or very slightly elevated systolic level, but a lower than normal diastolic level, so that the pulse pressure is elevated. The average pressure levels range between 140 and 150 systolic and 60 to 75 diastolic. Where there is coexisting essential hypertension, both levels are elevated, but the elevation in the systolic level is always relatively greater than the elevation in the diastolic.

The pulse rate corresponds, of course, to the heart rate when simple tachycardia is present. In the presence of auricular fibrillation and a rapid ventricular rate, there is the usual pulse deficit In all uncomplicated cases, the pulse is full and bounding, in some cases almost resembling

that of aortic insufficiency. There may even occur the pistol shot and the Duroziez signs, described in Chapter XXIV.

In the presence of coronary disease with the anginal syndrome as well as in congestive failure, the coexistence of mild thyrotoxicosis may be an underlying factor for the continuation of symptoms. This is often overlooked because of the prominence of the cardiac symptoms. The condition is spoken of as "masked thyrotoxicosis." The author has seen several cases of arteriosclerotic and hypertensive heart disease with congestive failure that were given up as hopeless, with the anticipation of early death, and where a masked thyrotoxicosis was one of the factors that was responsible for the failure Removal of this factor by proper medical preparation and surgery gave immediate relief from decompensation, and prolonged the life of the patient by many years.

Aids in Diagnosis

The recognition of thyrotoxicosis complicated and masked by other forms of heart disease with congestive failure, may be helped by the following tests and findings

The Digitalis Test· The patient is given a sufficiently large amount of a potent digitalis preparation which under ordinary conditions should result in a slowing of the ventricular rate, especially in the presence of auricular fibrillation If the ventricular rate is not slowed, thyrotoxicosis should be suspected, provided active infection or tissue destruction of the heart, or elsewhere in the body is ruled out

The Iodine Test Lugols solution, in ten minim doses is given three times a day for several days. The heart slows considerably at the end of that time in the presence of thyrotoxicosis

The Basal Metabolic Rate Determination A rate of more than plus 20 per cent is a suspicious finding, but is far from corroborative. In fact, rates as high as plus 40 per cent or even plus 50 per cent may occur in hypertension and especially in congestive failure in the absence of thyrotoxicosis Hamilton[13] observed a rate of plus 64 per cent in a case of congestive failure without thyrotoxicosis Nevertheless, any rate above normal, if persistent, after congestive failure has subsided, or other causes have been eliminated, assumes significance Contrariwise, a lower than the minimal normal rate certainly helps to eliminate the possibility of thyrotoxicosis

The Circulation Time. In uncomplicated thyrotoxicosis, the arm-to-tongue time is greatly shortened In congestive failure due to any cause, it is greatly prolonged If thyrotoxicosis coexists with congestive failure, the circulation time may either be normal or even shortened because the thyrotoxic element.

The Blood Cholesterol: This is always diminished in thyrotoxicosis.

In hypertension and in congestive failure, it is usually increased far above the normal level. If diminished in the presence of the latter conditions, thyrotoxicosis is to be suspected

Pigmentation of skin often occurs in thyrotoxicosis. Hamilton stresses it as an important sign It consists of a uniform brownish staining confined to the eyelids and a uniform dark pigmentation over the whole body resembling a sun tan. Some patients present sharply defined areas with less pigmentation, irregularly distributed. It occurs mainly in those cases which have congestive failure The condition, however, is not confined to thyrotoxicosis

The differentiation of thyrotoxicosis from psychoneurosis, which may closely simulate it, may also be helped by some of the above tests. In borderline cases, however, these two conditions may be very hard to differentiate, one from the other In *psychoneurosis* there are, usually, some other neurotic symptoms present by which it may be recognized, as discussed in Chapter XXIX.

Prognosis

Thyrotoxicosis may exist in a mild form for many years with fair comfort and may, in some cases, be overlooked, unless it is kept in mind. The severer forms, if neglected, may eventually result in congestive heart failure and death. Some may die from intercurrent disease superimposed upon the exhaustive state, which the disease produces.

Treatment

The treatment of thyrotoxicosis depends upon the severity of the disease. In the mild grades, medical therapy may be fully effective In the more severe forms combined medical and x-ray therapy may relieve the condition, although surgical removal of the thyroid is the most reliable measure

Medical Therapy· This consists of complete bed rest for several weeks, the use of a high caloric diet, consisting mainly of carbohydrates, and the employment of sedatives, such as the bromides, and if necessary the barbiturates. The bed rest must be absolute and there must not be any mental disturbance of any kind For this reason it is preferable to have the patient in a hospital or private sanitarium away from any disturbing home environment. Annoying visitors are not to be allowed to see the patient.

The effect of therapy is to be gaged by an increase in the weight of the patient, the disappearance of symptoms and the return of the basal metabolic rate to normal. If treatment is properly carried out, recovery may take place even in occasional cases where surgery fails.

Within the past few years, thiouracil and later propyl thiouracil came into use in the treatment of this disease It is based on the original observations of Mackenzie and co-workers[14] that sulfanilyl-quinidine, and later by Mackenzie and Mackenzie,[15] that sulfonamides and thioureas interfere with the production of thyroid hormones in animals Astwood[16] was first to report the use of thiourea and thiouracil in the human He administered it in three cases of thyrotoxicosis and obtained relief of symptoms, and a return to normal of the serum cholesterol and of the basal metabolic rate Many other cases have subsequently been treated by other observers with similar results

Some reports soon began to appear in the literature of the toxic effect of thiouracil in the production of granulopenia and even fatal agranulocytosis In 96 treated cases reported by Fishberg and Vorzimer,[17] 20 per cent showed granulopenia and one case developed typical agranulocytosis Other toxic effects were also noticed Thus, in the treatment of 43 cases by this drug, Gargill and Lesses[18] observed 2 cases who developed jaundice, 2 drug fever, 2 submaxillary gland swelling, 1 fatal agranulocytosis and 1 nonfatal granulocytopenia Other untoward effects observed by various clinicians were edema, urticaria, vomiting, abdominal pain, diarrhea and allergic arthritis

When carefully used, and the blood is frequently examined to detect the early appearance of granulocytopenia, the drug has great value in the treatment of this disease Prolonged remissions and even cures have been reported. It takes, however, about two or three weeks of treatment before its full effect is exhibited The reason is that the storage depots of thyroid hormone are not exhausted by the drug until that time

The safer, and perhaps more potent preparation is propyl-thiouracil, which is the drug used by the author It may be given in doses of 50 to 75 milligrams, three times daily for two weeks, then the amount is reduced to about 25 milligrams, three times daily as a maintainance dose A blood count should be done every three to seven days, and we must watch for any of the toxic manifestations

The length of treatment depends upon the response In most severe cases the drug is best used only in preparation for operation which may be the only cure

Radiotherapy Roentgen ray therapy in thyrotoxicosis has been practiced for many years with favorable results in a good proportion of cases Means and Holmes[19] obtained cures in one-third of their cases, relief in another third and no effect in the rest

Recently Herz and Roberts[20] and Chapman and Evans[21] employed radioactive iodine in the treatment of the disease The former authors used 5 to 25 and the latter, 14 millicuries, carried in one milligram or

less of iodine. This is approximately equivalent to a full dose of roentgens. Most cases responded to one dose, but some cases required two or three doses.

These observers feel that this form of therapy is preferable to the orthodox x-ray therapy. It is given by mouth and there is no danger of possible x-ray burns of the skin

The untoward reaction, at times, may resemble x-ray sickness, and fibrosis of the thyroid has been produced by this method in two cases, the same as occurs in x-ray therapy. Patients sensitive to iodides or thiouracil have been found to respond well to this treatment.

It is, perhaps, too early yet to decide the value of this therapy as a permanent cure. It appears to be, however, at least as efficacious as x-ray therapy, and those that are permanently cured by x-ray may similarly respond to this method of therapy

Surgical Treatment: This consists of a subtotal thyroidectomy, although in some serious thyrotoxic cases with severe cardiac disease a total thyroidectomy may at times be advisable. This is particularly essential where thyroid malignancy is suspected.

Thyroid surgery is not contraindicated in the presence of cardiac disease no matter how grave. The relief in most such cases is spectacular. If thyroidectomy is not done, many succumb to congestive failure

The patient must be carefully prepared for operation by bed rest and reassurance It is, perhaps, wise in some very apprehensive cases not to tell them that an operation is necessary. The barbiturates are to be given in sufficient dosage to help keep the patient relaxed. Lugols solution, ten minims, and propylthiouracil, 75 milligrams are given three times daily for several days to reduce the basal metabolic rate to as low a level as possible If auricular fibrillation and cardiac decompensation are present, proper digitalization is necessary before operation. Many of these patients require larger amounts of digitalis for proper therapeutic effect than similar cases without thyrotoxicosis.

Hypothyroidism

This condition, known as myxedema if it occurs in adults, or cretinism if it develops in childhood, is the antithesis in every respect to that of hyperthyroidism

The condition may follow a total thyroidectomy. In cases where it develops spontaneously, the cause is not known.

General Symptomatology: This depends upon the degree of hypothyroidism. In the fully developed stage of the disease, the patient presents a characteristic expressionless and bloated appearance, a peculiar yellowish pallor, scantiness of hair on the scalp and eyebrows, and a thick tongue,

His speech is slow and the voice somewhat hoarse His hands are spade-like and fingers thick The skin is dry, cold, coarse and thickened or puffy. There is mental dullness and general weakness

The Circulation in Hypothyroidism: Because of the markedly diminished metabolic state in this disease, the demand for blood is greatly diminished as is the total volume of the circulating blood The minute volume output is greatly decreased due to slowing of the heart rate, diminished amplitude of cardiac contraction, and the diminished venous return to the heart. In a study of a series of cases with total thyroidectomies, Altschule and Volk[23] found the minute volume output per square meter of body surface to be 1.1 to 1 4 liters in contrast to the normal of about 2 2 liters They also observed that the cardiac output is diminished proportionately more than the oxygen consumption, resulting in a rise of the arterio-venous oxygen difference

Lange[24] found a marked increase in the permeability of the capillaries in five cases of myxedema Under thyroid therapy, the permeability decreased with simultaneous increase in diuresis He believes that the serous effusions, the interstitial edema of the heart and the general body swelling observed in this disease are due to the increase in capillary permeability.

The Heart in Hypothyroidism The heart is usually enlarged in this disease. The enlargement appears to be diffuse. As seen fluoroscopically, the heart appears to sit squat on the diaphragm, the lower borders spread out so that the transverse diameter is markedly widened. The amplitude of cardiac contraction is greatly diminished, the movements of the border being hardly visible.

The underlying cause of cardiac enlargement in this disease is not definitely known Myxedematous infiltration of the heart wall and, perhaps, the presence of some pericardial effusion which is found in occasional cases, may partly be responsible for the enlargement. The main factor appears to be some degree of cardiac dilatation, found in many cases The dilatation may be caused by diminished tonicity of the heart muscle, and in some cases by a coexisting secondary anemia

Congestive failure occurs infrequently in hypothyroidism In a review of the literature, Ayman and co-workers[25] found less than 30 per cent of cases who showed signs of congestive failure A greater percentage complained of shortness of breath on exertion as an isolated symptom, but in most of these, no evidence of the so-called myxedema heart was found Hence, the shortness of breath could not be attributed to heart involvement The comparative infrequency of heart failure in hypothyroidism is probably due to the diminished work the heart is called upon to do

The anginal syndrome, likewise, rarely occurs in hypothyroidism, except when coronary sclerosis is present in addition. Even in such cases, the anginal syndrome may, in some instances, first appear when thyroid therapy is instituted.

The electrocardiographic evidence of cardiac involvement consists of very low voltage initial ventricular complexes with isoelectric or negative T waves, as was described elsewhere[25]

Aids in Diagnosis of Hypothyroidism: A frank, well developed case of myxedema or cretinism offers no difficulty in diagnosis In less advanced cases, where the findings are not clear cut, the diagnosis may be helped by determining the basal metabolic rate, the blood cholesterol, the circulation time and the use of the thyroid therapy test.

The *basal metabolic rate* is always low in this disease. In the presence of suspected signs and symptoms, a rate lower than minus 15 or 20 helps confirm the diagnosis, although such rates, and even lower rates may occasionally be found in some normal individuals

The *blood cholesterol* is always increased considerably above the upper limit of normal

The arm-to-tongue *circulation time* is greatly prolonged in this disease It may be double or more than the upper limit of normal.

Thyroid Therapy This is one of the best diagnostic tests of the presence of thyroid disease, and the only effective therapeutic measure. All signs and symptoms begin to clear under appropriate dosage of thyroid substance Care must be taken not to give too big a dose at first, especially in the presence of marked coronary or myocardial disease, because it may precipitate attacks of congestive failure or of the anginal syndrome

It is advisable to start with an initial dose of one-half to one grain of a potent thyroid substance daily, watching its effect carefully. The dosage may then gradually be increased to three grains daily, if no improvement is noted within two or three weeks It should be discontinued at once if symptoms of overdosage develop, such as palpitation, precordial pain, nervousness, or muscular cramps in the extremities. When these symptoms subside, the therapy may be resumed in smaller doses.

Under this therapy there is improvement in the physical and mental state of the patient, a progressive diminution in the size of the heart, a rise in the basal metabolic rate, and a lowering of the blood cholesterol.

Disease of the Suprarenal Glands

The circulation may be affected either by hyperfunction of the medullary portion, or by hypofunction of the cortical portion of the suprarenal glands.

Medullary Hyperfunction

Mechanism: As a transient manifestation, medullary hyperfunction occurs in conditions of extreme rage, emotional excitement and fear These factors stimulate the adrenal glands via the autonomic nervous system and produce an outpouring of adrenalin into the circulation

Manifestations. The symptom complex is characterized by marked palpitation of the heart, and in some cases, by the anginal syndrome The heart rate is greatly accelerated, and the blood pressure is elevated The amplitude of cardiac contraction is increased, the basal metabolic rate is raised, and there is marked irritability, sweating and occasional shortness of breath Transient hyperglycemia and glycosuria may occur, due to conversion of liver glycogen into glucose The manifestations are similar to those observed in hyperthyroidism, but are of transient nature, lasting only as long as the exciting factor is present The symptom-complex may be reproduced by injecting adrenalin in sensitive individuals

Paroxysmal attacks of the above symptom-complex and a hypertensive crisis have also been observed to occur spontaneously in tumors of the adrenal medulla, as described in Chapter XVII Each attack lasts a variable period Between the attacks, the patient is practically symptom-free

Treatment The essential therapy in this condition is to avoid sudden outbursts of emotional excitement This applies, especially, to those individuals with instability of the autonomic nervous system

Where the crises are caused by a suprarenal tumor, surgery must be resorted to

Cortical Hypofunction Addison's Disease

Pathology This condition is caused by any disease which destroys the cortical portion of the adrenal glands In about 60 per cent of cases, tuberculosis is the underlying cause In the rest, such conditions as atrophy of the glands, pyogenic infections, syphilis, fatty degeneration, metastatic malignancy or vascular disease may be causes

Manifestations The disease is characterized by general asthenia, pigmentation of the skin and mucous membranes, best seen in the oral cavity, progressive wasting, anorexia, nausea and vomiting, and occasional diarrhea The onset is usually insidious with progressive increase in the symptoms and periods of exacerbations and remissions

The cardiovascular abnormalities consist of marked hypotension, a diminished intensity of the heart sounds and a decrease in the amplitude of cardiac contractions During a crisis, which occurs in an acute exacerba-

tion, there is evidence of marked peripheral vascular failure or shock. The circulating blood volume is diminished due to loss of plasma, resulting in a decreased return of venous blood to the heart. The stroke volume is therefore markedly diminished producing a profound drop in the arterial blood pressure

According to Swingle and co-workers,[26] the shock in this disease is not relieved by the administration of fluids in contradistinction to other forms of reversible shock, but it is relieved by the injection of the cortical extract of the suprarenal gland. With the demonstration by Marine and Baumann[27] that the sodium content of the blood is lowered after suprarenalectomy, it is believed that the shock in Addison's disease is due to depletion of sodium from the blood

The work of Loeb and co-workers[28] tends to corroborate this impression. Injecting cortical extract in patients with Addison's disease prevents the elimination of the sodium Also the administration of large amounts of sodium chloride, even without the addition of cortical extract, gives considerable relief from symptoms in reversible cases.

Treatment The ideal therapy of Addison's disease might be the grafting of a suprarenal gland This has been accomplished in one case by Broster and Gardiner-Hill[29] who obtained such a gland from a patient with a hyperplasia of the adrenals, and implanted it into one with Addison's disease Symptomatic relief was obtained and the patient was still well four months later, when the report was submitted

The possibility for such successful therapy, however, is small for it is very seldom that a fresh adrenal gland can be obtained for grafting. There is also the possibility that the graft will not be successful

In the last few years extracts of the whole adrenal gland have been prepared and have been found effectual The cost, however, is very high

With the development of desoxycorticosterone acetate which is a synthetic factor of the adrenal gland the treatment of the disease has been greatly facilitated The substance is not a complete replacement therapy, however, although it has a definite effect in helping the retention of salt and water, and in alleviating the symptoms

The treatment of Addison's disease with desoxycorticosterone acetate, as recommended by Kemper,[30] is as follows: a daily dose of 3 to 6 grams of sodium chloride is given Desoxycorticosterone is injected in daily increasing doses until an amount is reached which gives symptomatic relief. Pellets of this substance, each weighing 125 mg are then implanted under the skin. The number of pellets to be implanted depends upon the requirements. Thus, 125 mg gives off approximately 0.5 mg of the hormone in 24 hours If the patient requires 5 mg. daily, the implantation of 10 pellets would be necessary to supply that dosage. Should a crisis

develop at any time, supplemental sodium chloride and adrenal extract are given in addition.

Thompson[31] recommends the use of testosterone propionate in addition to replacement therapy in this disease It improves the general vigor of the patient.

It has recently been demonstrated by various observers that desoxycorticosterone may produce temporary hypertension in Addison's disease, and also when given in some cases without adrenal disease The author has also observed it in two cases. Perera and co-workers[32] found that this increase in blood pressure can not be correlated with abnormal retention of the sodium iron in the blood or with an increase in the circulating blood volume. It is also apparently not dependent on the abnormally labile peripheral vascular system as measured by the cold pressor test Its mechanism is obscure.

De Gennes and co-workers[33] suggest that the induced hypertension might be due to a hypersecretion of the adrenal cortex caused by the substance. Sinatko and Necheles[34] have observed the development of liver necrosis when large doses of desoxycorticosterone are given to dogs This is enhanced by the addition of salt

Disease of the Pancreas

Disease involving the islands of Langerhans of the pancreas may affect the circulation. Insufficient secretion of insulin by this portion of the gland results in diabetes mellitus Excessive secretion produces hypoglycemic shock

Diabetes Mellitus

The early onset of arteriosclerosis in diabetes mellitus leaves no doubt that there is some causal relationship between the two diseases We do not, as yet, definitely know, however, how the diabetic state operates in the production of vascular disease Indeed, diabetes occurring in late life may be caused by arteriosclerosis, rather than be the cause of it That is, arteriosclerosis probably causes degeneration of the islands of Langerhans, resulting in a diminution in the secretion of insulin and thus, the diabetic state

Whatever the mechanism of the relationship of diabetes and arteriosclerosis may be, the occurrence of the two conditions in any patient calls for special care in the management of the case This is particularly true when the heart is greatly affected by coronary disease In such cases, inadequate control of the diabetic state may aggravate the cardiac status and may interfere with the proper action of the various drugs used in the relief of cardiac symptoms On the other hand, a sudden drop in

the blood sugar by the injudicious and careless use of insulin may seriously affect the heart, reducing or accentuating the anginal syndrome or congestive failure

Treatment: The treatment of the diabetic cardiac patient calls for the maintainance of as close to a normal blood sugar level as possible, and prevention onset of acidosis In most cases, it is not wise to attempt to maintain a normal fasting blood sugar of 100 to 125 milligrams per 100 cubic centimeters of blood by the use of insulin, for hypoglycemia may suddenly develop at one time or another, regardless of how carefully insulin is given Fasting blood sugar levels of 125 to 180 milligrams are well tolerated If such levels can be maintained without insulin, it is, perhaps, better not to use it, or certainly to use it very sparingly *In many cases, however, it is essential to use about 200 to 250 grams of* carbohydrate per day in order to prevent the possible onset of acidosis, and to supply the necessary glycogen to the heart If this amount together with about 70 grams of protein results in higher fasting blood sugar levels than 180 milligrams, and there is a loss of about 30 to 40 grams of sugar in the urine per twenty-four hours, we must resort to the use of insulin

The total caloric intake per day depends upon the activity of the individual, and the presence or absence of obesity In an active person, requiring about 2,000 calories per day, 250 grams of carbohydrates and 70 grams of protein, each yielding about 4 calories per gram will supply about 1,280 calories The remaining 720 will have to be supplied by fat, the caloric value of which is about 9 calories per gram That is, about 70 grams of fat will have to be added to make up the 2,000 calories

There is no set rule in the use of insulin in the cardiac case We may start with about one unit of insulin per each 2½ grams of sugar, which is eliminated in the urine per twenty-four hours If the response is not sufficient, we then slowly increase the insulin very carefully Globin insulin, given in the morning, is perhaps safer than plain insulin, as the fluctuating blood sugar levels are not so marked It is also safer than protamin zinc insulin which often shows its greatest effect in the middle of the night when it may result in hyperglycemic shock at a time when no immediate aid may be obtainable

The treatment of diabetic acidosis calls for large amounts of glucose and fluids to be given together with a sufficient supply of insulin

Hypoglycemic Shock

This is an important cause of an occasional acute circulatory collapse. It is characterized by marked tachycardia together with other symptoms such as trembling, nervousness, cold, clammy perspiration, a sense of hunger, drowsiness, headaches and even convulsions and death in severe

cases This may be produced by the excessive and careless use of insulin in the treatment of diabetes mellitus In rare cases, however, it may arise spontaneously as a result of some new growths of the pancreas which produce excessive secretion of insulin It may also be observed occasionally in endocrine disturbances other than that of the pancreas, as in Addison's disease, in myxedema, or in pituitary disease In these conditions there is a physiologic diminution in the antagonistic effects of the respective endocrine substances to insulin In occasional cases it may apparently occur as a result of vegetative nervous system disturbances

The treatment of hypoglycemic shock calls for the immediate supply of large amounts of sugar

Cardiovascular Abnormalities in Beriberi

Causes: Beriberi is primarily a disease of vitamin B_1 deficiency, but patients with this disease often present evidence of a deficiency of other vitamins, and products of nutrition It is very frequent in the Orient, but is also occasionally observed in other parts of the world In this country it is seen most often in alcoholics, but it may occur in other conditions where the diet is unbalanced, or the food improperly utilized Thus, it may occasionally occur in constitutional diseases requiring a restricted diet, such as gastric ulcer, diarrhea, or diabetes It may also occur in conditions of excessive metabolic activity such as in thyrotoxicosis, febrile diseases, and excessive physical strain

Clinical Manifestations These depend upon the severity of the disease In mild cases, there may merely be some dyspnea, palpitation and tachycardia on exertion and pretibial edema In more severe cases, these symptoms become more marked and signs of right heart failure may develop Generalized peripheral nonpitting edema may, at times, occur, giving the patient the appearance of a stout, robust individual In such cases it is due probably more to the reduction of plasma protein than to right heart failure The liver enlargement in the alcoholic is due mainly to cirrhosis

The *heart* may become enlarged, a gallop rhythm may develop and various murmurs may appear The arterial blood pressure is usually normal, although in some cases there may be an elevation in the systolic pressure and a depression in the diastolic, resulting in some increase in the pulse pressure Under the effect of comparatively little trauma or infection, the shock syndrome may develop

The cardiovascular manifestations are thus not characteristic of this particular disease Beriberi should be suspected if no other cause is found, and where other manifestations of the disease occur These are.

polyneuritis, tingling of the hands and feet, "tightness" of certain muscle groups of the extremities, loss of reflexes, the development of lameness, hand and foot drop, glossitis, red palms of hands, and various gastrointestinal disturbances.

Dock[35] ascribed some cases of cardiac hypertrophy, myocardial fibrosis with mural thrombosis in the heart to chronic beriberi affecting that organ.

Treatment: The treatment of beriberi heart disease calls for the administration of large amounts of vitamin B complex, especially B_1 The latter should be given in 25 to 50 milligram doses intravenously three times a day, while a sufficient amount of vitamin B complex is given orally When symptoms subside, the amount may be diminished. Digitalis and the mercurials are of no value in this disease The diet should be well balanced and must be rich in vitamins The use of alcohol should be prohibited in those cases where the underlying cause is chronic alcoholism

REFERENCES

1 Coffen, T H.: The incidence of heart disease in the Pacific Northwest. Am. Heart J 5 99, 1929

2 White, P D, and Jones, T D Heart disease and disorders in New England Am. Heart J. 3 302, 1928.

3 Burwell, C S, Smith, W. C, and Neighbors, DeW.: Output of heart in thyrotoxicosis, with report of case of thyrotoxicosis combined with primary pernicious anemia. Am J. M Sc 178: 157, 1929.

4 Boothby, W. M., and Rynearson, E H: Increase in circulation rate produced by exophthalmic goiter compared with that produced in normal subjects by work Arch Int Med. 55 547, 1935

5 Blumgart, H L Velocity of blood flow in health and disease, Velocity of blood flow in man and its relation to other measurements of circulation Medicine 10 1, 1931

6 Thompson, W O Studies in blood volume Blood volume in myxedema with comparison of plasma volume changes in myxedema and cardiac edema J. Clin Investigation 2.477, 1926

7 Lewis, J K, and McEachern, D · Persistence of accelerated rate in isolated hearts of thyrotoxic rabbits Response to iodides, thyroxine and epinephrine Proc. Soc Exper Biol & Med 28 504, 1931

8 Means, J. H. and Richardson, E Disease of the Thyroid Oxford Monographs on Diagnosis and Treatment London, Oxford University Press, 1929

9 Friedberg, C. K., and Sohval, A R The occurrence and the pathogenesis of cardiac hypertrophy in Graves' disease Am Heart J 13 599, 1937

10 McEachern, D, and Rake, G Study of morbid anatomy of hearts from patients dying with hyperthyroidism Bull. Johns Hopkins Hosp 48 273, 1931

11 Simonds, J P., and Brandes, W. W.· Size of heart in experimental hyperthyroidism. Arch Int. Med 45 503, 1930

12 Likoff, W. B, and Levine, S A. Thyrotoxicosis as the sole cause of heart failure Am J M Sc. 206.425, 1943

[13] Hamilton, B. E · Heart failure of the congestive type caused by hyperthyroidism. J.A M.A. 83·405, 1924

[14] Mackenzie, J. B, Mackenzie, C G, and McCollum, E. V. Effect of sulfanilyl-quinidine on the thyroid of the rat Science 94·518, 1941

[15] Mackenzie, C G, and Mackenzie, J B Effect of sulfonamides and thioureas on the thyroid gland and basal metabolism. Endocrinology 32 185, 1943.

[16] Astwood, E B: Treatment of hyperthyroidism with thiourea and thiouracil J A M.A 122·78, 1943

[17] Fishberg, E A and Vorzimer, J Extrathyroid effects of thiouracil therapy. J.A M A 128·915, 1945.

[18] Gargill, S L, and Lesses, M F. Toxic reactions to thiouracil J A M A 127 890, 1945

[19] Means, J. H, and Holmes, G W Further observations on the roentgen ray treatment of toxic goiter Arch Int Med 31 303, 1923.

[20] Herz, S, and Roberts, A Radioactive iodine in the study of thyroid physiology. VII The use of radioactive iodine therapy in hyperthyroidism J.A M A 131 81, 1946

[21] Chapman, E M, and Evans, R D The treatment of hyperthyroidism with radioactive iodine J A M A 131 86, 1946

[22] Altschule, M D, and Volk, M C Therapeutic effect of total ablation of normal thyroid on congestive failure and angina pectoris Arch Int Med 58 32, 1936

[23] Lange, K · Capillary permeability in myxedema Am J M Sc 208 5, 1944

[24] Ayman, D, Rosenblum, H, and Falcon-Lesses, M · "Myxedema heart" without evidence of cardiac insufficiency J A M.A 98 1721, 1932

[25] Sigler, L. H The Electrocardiogram, Its Interpretation and Clinical Application New York, Grune & Stratton, 1944

[26] Swingle, W. W, Pfiffner, J J, Vars, H M, Bott, P A, and Parkins, W. M Function of adrenal cortical hormone and cause of death from adrenal insufficiency Science 77 58 1933

[27] Marine, O, and Baumann, E J Duration of life after suprarenalectomy in cats and attempts to prolong it by injections of glucose and glycerol Am J Phys 81 86, 1927

[28] Loeb, R F, Atchley, D W, Gutman, E B, and Jillson, R On mechanism of sodium depletion in Addison's disease Proc Soc Exper Biol & Med 31 130, 1933

[29] Broster, L R, and Gardiner-Hill, H Case of Addison's disease successfully treated by graft Brit M J 2 570, 1946

[30] Kemper, C F Treatment of Addison's disease by implantation method Ann Int Med 22 161, 1945

[31] Thompson, W O Uses and abuses of the male sex hormone J A M A 132 185, 1946.

[32] Perera, G A, Knowlton, A I, Lowell, A and Loeb, R F Effect of desoxycorticosterone

...sion in

1947

[34] Sinaiko, E S, and Necheles, H Liver damage by desoxycorticosterone. Science 109. 37, 1949

[35] Dock, W Marked cardiac hypertrophy and mural thrombosis in the ventricles in beriberi heart Tr Am Phys 55 61, 1940

CHAPTER XXIX

Psychosomatic Cardiovascular Abnormalities

UNDER this heading we shall discuss a variety of cardiovacsular disturbances not caused by structural disease of the heart and blood vessels If structural disease is also present, it is either not of sufficient degree, or is not the type that would produce the multiple disturbances which the patient presents

CLINICAL FORMS

The condition *may* occur *either* as *a purely subjective phenomenon* or there may also be many abnormal objective findings

In the purely subjective group, the patient develops a varying degree of apprehension, and at times a morbid fear of heart disease without any objective manifestations of such disease.

The condition may occur in a normal individual as a temporary phenomenon, after witnessing the sudden death of a relative or friend from heart disease, or after having been told by an examining physician that there is something wrong with his heart It is more apt to occur in individuals who know that they have some organic heart disease. Simple reassurance is often enough to overcome the apprehension

In a more severe and protracted form, it may occur in individuals who present various other psychoneurotic disturbances Here, reassurance may be of no avail, and they often become serious problems in therapy.

In those who present objective abnormalities in addition to the subjective complaints, the disturbances appear to occur through the intermediation of the vegetative nervous system This condition has been variously labeled by different authors as "the irritable heart of soldiers," "disordered heart action," "effort syndrome," or "neurocirculatory asthenia"

In a recent monograph Friedman[1] expresses his opinion that all these titles are inadequate to describe the symptom-complex of the disease, and suggests the use of the term "functional cardiovascular disease." However, inasmuch as the term "functional" is usually employed in classifying patients with heart disease as to their ability to carry on activity, this title has its drawback The *all-inclusive* "psychosomatic cardiovascular abnormalities," used as the heading of this chapter, is perhaps more descriptive

SUBJECTIVE MANIFESTATIONS

These may consist of precordial pain, palpitation, respiratory disturbances, faintness, dizziness, ringing or pounding in the ears, flashes, tingling or other sensory disturbances, fatigue, sweating, anorexia and tremors.

The Precordial Pain: The precordial pain here differs from angina pectoris in many respects. It does not appear on exertion, but is usually spontaneous. In fact, in some cases it diminishes or entirely disappears during physical activity It is usually located in the left precordial rather than in the retrosternal region, and is described either as a soreness, or as a sharp, darting stabbing, or a needle-like pain It may radiate to the left arm

Palpitation: This is usually described by the patient as a "thumping" in the heart region, a "sensation of very rapid heart beat," a "skipping of beats," or as "irregular beats" Examination of the heart may reveal premature contractions or even paroxysms of auricular fibrillation or tachycardia during the time when these sensations are experienced.

Respiratory Disturbances These usually consist of the inability of the patient to take a deep breath, with a feeling that not enough air enters the lungs. In an attempt to overcome this feeling, the patient often presents a very rapid respiratory rate, and the respirations are very shallow Friedman[1] observed that 80 per cent of these cases use predominantly costal breathing, the diaphragm remaining practically unused, especially in waking hours He attributed the respiratory disturbances as well as the dull precordial pain to diaphragmatic inertia In rare cases, the marked hyperpnea, which these cases develop may result in hyperventilation tetany or syncope.

Faintness, Dizziness and Ringing in the Ears These are frequent manifestations They are probably due to transient local cerebral circulatory disturbances, and not to lessened forward propulsion of blood by the heart. The same may be said of the *flashes*, *tingling*, or other sensory disturbances

Fatigue. This symptom is described by the patient as severe physical tiresomeness, weakness, exhaustion or general lack of energy Many patients complain also of "mental exhaustion" with lack of interest for anything or anybody There is a desire to be left alone

Anorexia· This is often associated with other gastro-intestinal disturbances such as nausea, vomiting, diarrhea and abdominal pain It may result in considerable loss of weight

Tremors: In occasional cases this may be prominent The patient experiences chills which shake the whole body, or local muscular tremors, especially of the hands, not unlike those of thyrotoxicosis

Physical Findings

In most cases the objective findings are insignificant and do not correspond to the wide variety of complaints. There may occur, from time to time, a moderate to a marked degree of flushing of the face, neck and upper chest which, with the tremors and sweating, as well as the anxiety, nervousness and loss of weight may resemble thyrotoxicosis

The heart is normal in size and is often hypoplastic and of longitudinal shape. In the presence of coexisting valvular, hypertensive or other organic heart disease the heart, may of course, be enlarged and may assume the configuration common to the given disease. The heart rate may be accelerated and, as said before, premature contractions and even paroxysmal tachycardia or transient auricular fibrillation may be observed The heart sounds are often markedly accentuated and a faint systolic murmur may be heard. The cardiac contraction is usually forceful, as felt by palpation and as seen fluoroscopically.

The lungs show no structural changes that would explain the respiratory embarrassment, and a vital capacity determination may yield normal findings

In some cases there may be a rise in the rectal temperature from time to time, to as high as 100 5 degrees F. and in rare instances, higher. This must be borne in mind, as the condition may be mistaken for early tuberculosis or endocarditis

Underlying Causes

The predisposing cause is a hereditary, neuropathic predisposition. In most cases there is a history of psychoneurotic or psychosomatic disturbances in parents, brothers, sisters or other members of the family. Where this predisposition is marked, the disease may exist in a chronic form all the time with periods of exacerbations by any provocative cause.

Besides the neuropathic predisposition many of these cases present a hereditary inferiority in their constitutional state They cannot carry on the same amount of activity as a normal individual. As said before, easy fatiguability and lack of vigor are important manifestations of the disease.

Some of the *provocative causes* mentioned by Conner[2] are comments by a doctor in the course of examination that suggest the presence of organic heart disease or abnormality, the occurrence of a dramatic case of heart disease in the family with sudden death, the appearance of symptoms referable to the heart region leading to doubt as to its integrity; and some serious emotional stress.

In cases where the predisposition to the disease is not marked, a much greater emotional stress, life tragedy or calamity is necessary to bring

about an attack Cases were first observed in this country in large numbers during the Civil War and again during the First and Second World Wars. It was interesting to find during these periods that some men developed severe manifestations of the disease on the mere anticipation of being drafted, others before active induction in the army, and still others only after grueling experiences of army life Even in the last group of cases, some endured several prolonged battles before symptoms developed, others broke down almost immediately after they were moved to the front lines These facts demonstrate the variations in the reaction among different individuals to the same emotional stresses and strains

In civil life, an acute onset of the illness has been observed in some patients following the death of a member of the family, an automobile or other accident, a great financial loss, a disappointment in love, a family disruption and other severe disturbing factors As said before, it has also occurred after the patient was told that he had a heart murmur, high blood pressure or an abnormality in the electrocardiogram The last factor has in late years been a frequent cause. Misinterpretation of insignificant changes in the electrocardiogram or improper correlation of gross electrocardiographic abnormalities with the clinical findings in the case have often given the patient a serious fear complex

A typical example is a male, 31 years old who was subject to recurring spontaneous attacks of shooting and burning left precordial pain. He consulted a physician who found "abnormalities in the electrocardiogram" which supposedly indicated the presence of coronary disease. The patient was advised to give up his work and all forms of activity, and to have long hours of rest and relaxation Immediately after, the pain became much more severe and persistent, and he developed attacks of recurring palpitation, "air hunger," dizziness, and at times, severe fainting sensations with cold perspiration and pallor. These were considered by the doctor to be attacks of coronary occulsion, although at no time did the electrocardiogram confirm the diagnosis

A careful history revealed a neurotic and emotional tendency in other members of his immediate family The patient himself, was subject to emotional instability from early childhood There was some impairment in his capacity for decision and action He was subject to extreme anxiety states and showed an inferiority complex To overcome these he developed a capacity for considerable work, and had achieved moderate success in business at the expense of great effort He was married and had three children over whose future welfare he expressed great anxiety.

The physical examination revealed no evidence of structural cardiac disease The heart was of normal size and shape, the rate was about 80 beats per minute, and the rhythm was regular The heart sounds were accentuated, and no murmurs were present. His blood pressure

was 145, systolic and 90, diastolic. During an attack the heart rate varied between 100 and 130 beats per minute, the pulse was weak, and he presented considerable tremors of hands, marked sighing respirations which consisted of shallow respiratory excursions at a rapid rate The electrocardiogram showed no significant abnormalities. There was a tendency to left axis deviation, some rounding of the RT segment in the first and second conventional leads, and slurring at the bases of the R waves The precordial leads, likewise, showed no gross abnormalities.

He was reassured that his heart was perfectly sound, and was advised to resume his business, and also to engage in all open air sports. The underlying cause of his illness was explained to him to be a somatic reaction to an anxiety state He took the advice to return to activity, reluctantly at first, but after repeated reassurance, he finally returned to a normal life, and has been actively engaged ever since, now about fifteen years, with practically no symptoms The electrocardiogram remains persistently the same

Although in many cases a history of some known emotional stress can be obtained to explain the acute psychosomatic disturbances, in others no direct cause can be discovered by ordinary questioning. A more thorough inquiry into the life history of the individual from early infancy, through school life, adolescence, adult and marital life is necessary His reactions to his social and environmental conditions have to be analyzed In some cases, a serious emotional disturbance occurred in infancy, early life or later, which was buried in the subconscious mind and which finds expression from time to time in so-called "organ language" or somatic manifestations Many of these cases require careful study by a trained psychoanalist to unravel the hidden, mysterious mental elements which produce the somatic reactions

In some cases, the condition may be aggravated by physical strain, focal infection, toxic agents such as tobacco and coffe, as well as by reflex disturbances from the gastro-intestinal tract, gall bladder or other areas of the body These elements appear to have aggravating effects on the autonomic nervous symptom which is the underlying mechanism of the disease

It must be remembered that psychosomatic cardiovascular disturbances may also occur in cases who present organic disease of the heart and blood vessels, as said before In such cases we must determine the part played by the organic disease and that by the psychopathologic state in the production of symptoms This is very essential from a therapeutic viewpoint. For instance, the anginal syndrome due to coronary disease will respond to nitroglycerine, but precordial pain due to psychosomatic disturbances will be aggravated by the drug. Likewise, dyspnea due

to congestive failure will be relieved by the proper use of digitalis and, if necessary, by the diuretics, while psychosomatic respiratory disturbances will be aggravated by these drugs because they suggest to the patient the presence of heart disease.

Mechanism

Psychosomatic cardiovascular disturbances are thus seen to be brought about either by an evident or by a pent-up emotional state, hidden in the unconscious sphere. The manner in which these emotional states are translated into somatic disturbances is not as yet fully understood.

Based on experimental and clinical work within the past three decades we begin to look at the hypothalamic region as the seat of the emotional part of the mind, and the autonomic centers Thus, Cannon and Britton[3] produced "sham rage" by decorticating a cat The slightest provocation in such a decorticated animal would make it spit, scratch and bite Alpers[4] observed that certain organic lesions of the hypothalamus were capable of inducing personality and intellectual changes in the individual without discoverable cortical lesions Bricker[5] succeeded in stimulating the hypothalamic region of a conscious patient and has observed a rise in blood pressure, pulse and respiratory rates, and profound emotional outbursts.

Beattie and co-workers[6] demonstrated the existence of nerve tracts connecting the hypothalamus and spinal sympathetic centers Premature contractions of the heart induced by chloroform were abolished if the hypothalamus was divided in a plane between the anterior edge of colliculi and posterior edge of the pituitary fossa Stimulation of the posterior hypothalamus produced extra systoles if the sympathetic nerves to the heart or to the adrenal glands were intact

These are a few of a great many other interesting observations which suggest that the seat of the emotional part of the mind is probably in the hypothalamic region of the brain in close proximity to the autonomic nerve centers The translation of the emotions into somatic manifestations is probably accomplished by stimulation of these autonomic centers and the impulses are thence transmitted along the autonomic nervous system to the various parts of the body This undoubtedly applies also to the concealed or suppressed emotions, fears or anxieties which are probably stored in the subcortical portions of the brain, in the autonomic zones

Diagnosis

Psychosomatic cardiovascular abnormalities are very prevalent both as primary manifestations and as complications of organic cardiovascular

disease Dumbar,[7] in a study of 1600 hospital cases, mostly cardiac, with syndromes termed organic, found that 80 per cent had emotional difficulties which accounted for the manifestations. Most of them were relieved after 10 to 20 hours of psychotherapy Bennett[8] feels that this class of cases is inadequately recognized and poorly treated He considers the physician so organically minded that he fails to heed or learn He cites 150 cases with illness basically psychic which were not recognized until they developed into frank psychiatric syndromes.

The disturbance may often be confused with thyrotoxicosis If we bear in mind the criteria for diagnosis of the latter disease, as given in Chapter XXVIII, there should not be any difficulty in its differentiation

In those cases that present a low grade fever, we must rule out tuberculosis or endocarditis, either rheumatic or bacterial. The differential diagnosis of these conditions can usually be easily made after a short period of observation, using the criteria presented in Chapters XXII and XXIII.

Friedman[1] devised a hyperventilation test for use in the diagnosis of this disease It is partly based on previous observations by other authors that the breathholding time of these patients is usually reduced, and on the observation of Da Costa, known as Da Costa's syndrome, that no involuntary apnea follows prolonged deep breathing

Friedman's test consists of having the patient take a very deep inspiration and hold his breath as long as possible, noting the number of seconds which he is able to do so. Then have the patient breathe normally for 3 minutes, followed by taking 45 rapid breaths for 45 seconds. At the end of that time, have him hold his breath again as long as possible, noting the length of time he can do so. The figure he obtains by dividing the breath holding time in seconds, after the hyperventilation by the breath holding time before the hyperventilation, he calls the "hyperventilation index." He found that normal individuals have a hyperventilation index of 1.30 to 2 13, the average being 1 58 In individuals who complained of dyspnea in this disease the hyperventilation index is reduced to less than 1.30.

One of the diagnostic criteria of this disturbance is the presence of periorbital pigmentation in many cases, as in thyrotoxicosis.

Prognosis

This depends mainly upon the ease with which the symptoms develop If symptoms occur only after severe psychic trauma, while previously there were no manifestations of the disease, the prognosis is good Proper psychotherapy, as well as physical care will result in recovery. If it occurs in a severe form after a comparatively unimportant incident, and the

patient presented some mild disturbances before, the outlook is poor They usually go through life with the disturbances in a chronic form. Such cases have to be carefully guarded against some severe provocative factor. Individuals of this kind, for instance, should not be accepted for military service, even though, structurally, the cardiovascular system may be sound. They make poor fighting material, if they do not break down before they reach the firing lines, and they are a financial drain on the government in hospital care and in pensioning

Treatment

The primary therapeutic measure to be employed in this disease is proper reassurance. This can only be accomplished if sufficient interest is shown in the patient A great deal of attention is to be given to every *one of his complaints.* A careful physical examination and a complete laboratory check-up are to be made, for two reasons. One is to rule out any possible somatic disease that may account for, or may aggravate the symptoms of which he suffers Another is to impress the patient with our thoroughness, which will help to convince him that the complaints he has are not caused by his organic disease. If some organic disease is found he must be reassured that it is not the cause of his trouble

To the patient, his symptoms are real, and an attempt on the part *of the physician to belittle them or to laugh them off will seriously interfere* with therapy. On the contrary the patient must be told that all his symptoms have significance, and are real, but they are caused, not by structural disease of the cardiovascular system, but by functional disturbances. It may be wise to explain to the patient how certain ideas, fears, frustrations, worries, jealousies, disappointment and other emotional upset may be converted into disturbances of various organs, particularly the heart, which traditionally is supposed to be the seat of emotions.

Proper guidance as to the amount of physical and mental activity is of importance We must realize that we are dealing with individuals who are both physically and mentally inadequate to cope with environmental situations These must be, therefore, adjusted in the individual case to meet with his ability to carry on. To remove any possible inferiority complex that this adjustment may create, we must explain to the patient that the work capacity in different individuals varies greatly, and that some of the world's greatest deeds were accomplished by men who were physically not up to par

In many complicated cases where reassurance is of no avail, psychoanalysis and psychotherapy by a competent psychiatrist are essential

Drug therapy is of no value in this disease The use of any drug which is known to have some action on the cardiovascular system should be

strictly omitted, so as to prevent possible suggestion of the presence of organic disease. The sedatives may be of value, at times, when extreme nervousness is evident

REFERENCES

[1] Friedman, M Functional Cardiovascular Disease Baltimore, Williams & Wilkins Co, 1947.

[2] Conner, L A The psychic factors in cardiac disorders. J A M.A 94 447, 1930.

[3] Cannon, W B, and Britton, S W Studies on the conditions of activity in endocrine glands Pseudo affective medulliadrenal secretion Am J Physiol 72 283, 1925

[4] Alpers, B J Personality and emotional disorders associated with hypothalamic lesions Psychosom Med 2 286, 1940

[5] Brinker, R R Hypothalamic functions in psychosomatic interrelations. Psychosom. Med 1 19, 1939

[6] Beattie, J, Brown, G R, and Long, C. N. H Physiological and anatomical evidence for *the existence of nerve tracts connecting the hypothalamus with spinal sympathetic centers* Proc Roy Soc, London 5 106 253, 1930

Dumbar, F Psychosomatic Diagnosis New York, Paul B Hoeber, 1943

[7] Bennett, A E Faulty management of psychiatric syndromes simulating organic disease J A M A 130 1203, 1946

CHAPTER XXX

Pregnancy and Cardiovascular Disease

The presence of cardiovascular disease in the childbearing age poses the following very important questions: Should a woman with such disease be allowed to become pregnant? If she is pregnant what precautions are to be used, and what are the indications for its interruption. Does pregnancy have any aggravating effect on the existing cardiovascular disease?

In this chapter, we shall attempt to answer these and related questions regarding pregnancy and cardiovascular disease

Physiologic Effects of Pregnancy on the Circulation

To get some idea of the possible effects of pregnancy on a diseased heart, we must have some knowledge of the physiologic effects of pregnancy on the normal circulation. Although such knowledge is far from complete, a number of studies have been made by many investigators in recent years, which shed some light on the subject

Dieckmann and Wegner[1] as well as other observers before them found an increase in the blood volume, in the hemoglobin and in the hematocrit during pregnancy. At term, the average increase in the blood volume was 22.5 per cent, in the hemoglobin, 13 per cent, and in the hematocrit 20 per cent. They believe that these factors are part of a mechanism to avoid undue effort of the maternal organism to supply the proper gaseous metabolism of the fetus

The velocity of the blood flow, as determined by the circulation time measurements, has been studied by various observers. Their reports, however, are somewhat conflicting. Manchester and Loube[2] in a study of 48 pregnant women without heart disease during each trimester, found the volumes to be within normal limits. However, there was a definite tendency for progressive acceleration of the velocity of blood flow, as shown by the shortened circulation time, in the second and third trimester, although the figures were still all within normal range. They believe that if the circulation time is lengthened in the later months, it may be an early manifestation of decompensation.

Burwell[3] observed an increase in the basal heart rate of 12 to 20 beats per minute during the early part of pregnancy, but this rate diminished later. He also observed a slight rise in the pulse pressure, an increase of oxygen absorption in the lungs, an increased cardiac output per minute, an elevation in the venous pressure in the pelvis and legs, a low arterio-

venous oxygen difference of blood irrigating the placenta and uterus; and an increase in the total blood volume. On the basis of these findings, as well as a loud murmur heard at the placenta and some dilatation of the arteries at the velous spaces, shown by Spanner, the author concluded that the condition resembles the physiologic effects of an arterio-venous fistula.

Although the venous pressure is elevated in the legs and pelvis, it is not elevated in the upper part of the body during pregnancy. This was demonstrated by Thomson and co-workers.[4] They found the venous pressure in the arm to be normal throughout normal pregnancy but that it rises slightly in early puerperium returning to the early pregnancy level in the later postpartum period. The same is true in pregnant women with compensated heart disease In "toxemia" of pregnancy, there is only a slight increase in venous pressure

Widlund[5] studied the oxygen consumption, ventilation, blood pressure, heart rate and response to exercise in normal pregnant women and observed that at rest the findings were similar to those of nonpregnant women doing moderate work In other words, the pregnant woman utilizes her reserves even at rest

In a study of circulatory changes during and after obstetric labor in normal patients and in patients with heart disease, Brown and co-workers[6] found no consistent changes in the heart rate, blood pressure, vital capacity and circulation time The venous pressure was elevated significantly and often to abnormal levels during the first 24 hours after delivery. Such elevation could be attributed to the effects of ergotrate and probably also of pituitary preparations A hemotocrit and blood volume study indicated that a significant volume of fluid leaves the vascular compartment at about the time of delivery A greater volume returns to the blood stream on the second and subsequent days of puerperium A return to the normal nonpregnant blood volume probably occurs after this as a result of diuresis The authors agree with Burwell that the uterus at term contains a shunt of important proportions They also believe that the repeated uterine contractions of normal labor have the effect of temporary occlusion of the placental circulation thus preparing the cardiovascular system for permanent occlusion of the shunt They feel that for this reason, vaginal delivery is better tolerated than caesarean section by patients with serious heart disease.

Sampson and co-workers[7] estimated by an oxygen consumption study that the work of labor may at times be equivalent to climbing a seven foot flight of stairs every three minutes during a labor lasting 12 hours It may take an hour after delivery to repay the "oxygen debt" incurred during a long, hard second stage of labor.

It would appear, therefore, that the load thrown upon the circulation

by pregnancy is somewhat similar to that of an arteriovenous fistula in some part of the circulatory system, and is of considerable degree. According to Hamilton,[8] the load curve rises slowly up to the sixth month and then steeply to an average of about 50 per cent above normal and remains so until the last month, when it diminishes to about 25 per cent above normal, until term There are some deviations from the average load curve in different individuals. In some, the rise does not occur until the seventh month, and in others there is a decline before the last month.

Manifestations of Circulatory Disturbances in Pregnancy

Although the load of the circulation is markedly increased in pregnancy, normal women and well-compensated cases of heart disease carry it well in the vast majority of cases In an occasional case, either normal or cardiac, the increased blood volume and hemodilution may result in some dyspnea, palpitation, and in rare cases in a suffocating feeling and in pulmonary edema In some cases mild general puffiness all over the body may be observed. Such puffiness is probably due to some factor acting on the capillaries rather than to heart failure There may be some as yet unknown endocrine imbalance, avitaminosis or toxic state in pregnancy which affects the capillaries Another possible cause is the occurrence of a low plasma bicarbonate value resulting in mild acidosis. Osman[9] has shown that unexplainable edema may, at times, be due to low plasma bicarbonate which occurs ordinarily more often in females than in males, and most often in pregnant women

Due to increased load, slight cardiac enlargement may occur after the fifth month, even in normal individuals, and an increased enlargement in cardiac disease This, however, is often difficult to determine since the elevation of the diaphragm caused by the gravid uterus, places the heart in a transverse position which may be mistaken for enlargement. The high diaphragm is also partly responsible for the dyspnea

We often hear a systolic murmur in various areas, especially at the pulmonic area in such cases, even in the absence of cardiac disease In a follow-up of 73 apparently normal women through the entire period of pregnancy, Sodeman[10] found a transient pulmonic systolic murmur in 30, an apical and basal systolic murmur in 18, an apical alone in 6 One patient presented a high-pitched diastolic murmur at the aortic area

The occurrence of these murmurs in normal pregnant women may be due to a combination of factors such as the transverse position of the heart, cardiac acceleration, increased blood volume and hemodilution

Frank congestive failure in the presence of cardiac disease is seldom observed before the fifth month If it does occur, some underlying cause other than pregnancy is to be looked for, such as overstrain, infections, paroxysmal tachycardia, recurring rheumatic fever or insufficient

rest The same factors will precipitate heart failure much more frequently, and in a more severe form in the later months During that period, failure may even occur spontaneously

Forms and Incidence of Heart Disease in Pregnancy

The incidence of heart disease among pregnant women is very small. Hamilton found 1335 cases of heart disease in a series of 76,125 pregnancies, making an incidence of 1 8 per cent This is approximately the incidence of heart disease in the general population between the ages of 20 and 40 years, before the onset of arteriosclerosis

Because of the comparative rarity of arteriosclerosis during the years when pregnancy occurs, it does not enter into the etiology of heart disease in pregnancy It may contribute to the symptomatology and to the cardiac breakdown in occasional cases beyond 35 years of age, but rarely before

The most frequent form of heart disease in pregnancy is the chronic rheumatic, comprising about 90 to 94 per cent of cases. Next in frequency is the congenital group with about 2 to 5 per cent of cases The remaining cases consist of occasional thyrotoxic, hypertensive and syphilitic cardiovascular disease, infectious-pericarditis, bacterial endocarditis, paroxysmal tachycardias and other forms

Of the rheumatic group, the most common is mitral stenosis Next in frequency are mitral insufficiency, mitral stenosis and insufficiency and combinations of mitral and aortic valve disease Aortic insufficiency alone is very infrequent

We occasionally encounter a case of complete heart block, either congenital or acquired The author[11] reported one such case complicating pneumonia during the sixth month of pregnancy with successful termination Herman and co-workers[12] reported a case where heart block had existed since 20 years of age and the patient went through six successful pregnancies Quintin[13] reported a case with two successful deliveries, and quoted Jensen who found 14 such cases in the literature up to 1938.

Heart Disease as a Risk in Pregnancy

As said before, the majority of cases with heart disease may go through *pregnancy without any risk to the mother or off-spring The mere presence of such disease is, therefore, no indication for the prevention or termination of pregnancy.* There are, however, certain cardiac conditions and complications which carry a definite hazard to pregnancy These must be clearly recognized to guide the patient properly

The most important factor which contraindicates pregnancy is a poor *functional state of the heart.* This may be best ascertained by careful inquiry of the patient as to the amount of activity she can perform in her

daily life without discomfort. The classification of the functional state in any given heart disease has been described in Chapter XIII

Using this classification, it has been found that all individuals with heart disease who fall in class I or II almost invariably go through a normal pregnancy and delivery without discomfort. Few, if any, of these cases die as a result of their heart disease unless the classification changes during pregnancy due to reinfection, excessive strain or other factors mentioned before. Patients belonging to Class III often develop, during pregnancy, delivery or puerperium, congestive failure which occasionally results in death Those in Class IV invariably develop failure

Hamilton[7] calls attention to an occasional case of mitral stenosis without symptoms before or during pregnancy, who suddenly develops severe pulmonary congestion and hemoptysis with no known provocative cause The attacks may come on at any time during pregnancy, even before the sixth month when the load on the circulation is not excessively heavy Two of his cases ended fatally Termination of pregnancy in this group of cases has been followed by cessation or diminution of attacks These occurrences, however, are too rare to detract from the value of the classification as a guide

Severe *disturbances in rhythm* such as auricular fibrillation or flutter also constitute serious hazards In the author's personal experience of about 350 cases of cardiac disease in pregnancy, 12 developed auricular fibrillation during the pregnancy Of these, 2 died prior to delivery and 2 within several months after delivery from congestive failure, the mortality rate thus being 33 per cent In 379 pregnancy cases with cardiac disease reported by Bromwell and Longson,[14] 24 developed auricular fibrillation and seven of these died, with a mortality rate of 29 2 per cent Carr and Hamilton[15] reported 500 cases, in which 14 had auricular fibrillation with 6 deaths, the mortality rate being 42 9 per cent The over-all general mortality rate for the entire series of cases in each of these reported groups was slightly over 6 per cent This has been reduced in recent years to about 4 per cent

A third hazardous factor is marked cardiac enlargement, even if the functional state at the time of the examination is no worse than Class II An enlarged heart is the result of old and prolonged strain, or is the seat of degeneration, and a breakdown in its reserve is to be expected under the increased strain of pregnancy

Certain complications also carry serious risks Of these, the most important, because of its relative frequency is hypertension. In 218 hypertensive cases, with 301 pregnancies reported by Chesley and Annitto,[16] the maternal mortality was 20 times that of the whole hospital experience, the fetal loss was ten times, and toxemia was seven times that of normal controls

Another complication is subacute bacterial endocarditis. With the advent of penicillin therapy, the seriousness of this complication has been radically reduced. Hamilton[8] in answer to a questionnaire sent out to cardiologists and obstetricians obtained information on 17 women treated for subacute bacterial endocarditis with penicillin during pregnancy and puerperium. Nine of these died within five months following delivery with a total mortality rate of 53 per cent The fetal mortality was approximately 24 per cent Eleven cases who conceived after having been "cured" by penicillin, all survived Three of them were aborted and six had living children

An additional complicating factor is recurring rheumatic carditis. Inasmuch as this is far more frequent in the early twenties than later, the age element is important. In the younger age group, particular care is to be taken in an inquiry as to possible signs and symptoms that may point to acute reactivation, before pregnancy is allowed.

The age element is also a factor in determining if pregnancy is to be allowed Individuals in the late thirties and early forties are more apt to develop congestive failure with or without auricular fibrillation. In considering individuals at these ages, special care must be exercised in determining the cardiac functional state, and the potentialities for a breakdown Experience has shown that the mortality is higher in primiparas and in cases with multiple pregnancies, and lower in cases of para 2 to 4 The reason is that in primiparas there is a greater possibility of rheumatic recurrence and in multiple pregnancies the older age limits are reached when other complications are apt to set in

Classification of Cases as to Risk

To decide if pregnancy is to be allowed in any cardiac case, we must be guided by the extent of the cardiac lesion and size of the heart, the age of the patient, the presence of auricular fibrillation or other severe arrhythmia and the functional capacity of the heart Based on these findings we may classify all patients into the following three groups:

Group I: Individuals less than 35 years of age with valvular disease or a congenital defect who show no marked cardiac enlargement or a severe arrhythmia, and where the functional classification is Class I or at most Class II If the valvular damage is of rheumatic origin, and no recurrence of rheumatic fever has taken place within several years, pregnancy may be safely undertaken

Group II: Individuals with cardiac disease who show moderate to marked cardiac enlargement, recurring rheumtic fever within one or two years previous to the expected pregnancy or who present a low grade hypertension and a classification of Class III most of the time, although after rest, relaxation and good general care, they may revert to Class II.

To decide if pregnancy is to be allowed here we must consider the psychologic and economic aspects of the case. If the patient's psychologic makeup is such that she considers "life without a baby not worth living," as some of these cases often express themselves to the author, we may allow one, and in unusual instances, two pregnancies, provided the economic status is favorable The patient must be so situated as not to be required to do any housework, to have proper food, proper clothing and careful medical attention throughout pregnancy Under such circumstances the great majority of cases will go through pregnancy and delivery without complications If decompensation does set in at any time, it usually can be controlled by bed rest and digitalization

Group III: In this group are to be placed cases with marked cardiac enlargement, auricular fibrillation, moderate to marked hypertension, frequently recurring rheumatic fever, recurring congestive failure or other severe complicating conditions In such cases, pregnancy should be strictly prohibited and if it occurs, it should be terminated early. If the patient insists upon going through a pregnancy, the family should be warned of its grave danger, and the patient must get extremely careful medical supervision throughout the pregnancy, during the delivery, and the puerperium Even with all this care many of these cases succumb.

There are two other factors that have to be taken into consideration in our advice to the husband and wife for prospective pregnancy when either one or both have cardiovascular disease One is the possible transmisson of a poor hereditary soil to the offspring which may predispose the child to such disease at any time during its life This was discussed in previous chapters Although there is no conclusive evidence to prove that such hereditary transmission definitely exists, from clinical experience we know that this is true in many instances.

Another factor is the extra strain thrown on a patient with heart disease, in rearing a child This is true particularly in families of poor income, where all the burden of housekeeping is thrown on the mother

Management of the Cardiac Case

In the management of the cardiac cases in pregnancy, it is essential that the patient avoid all undue physical or mental strain and fatiguing engagements. Proper clothing is necessary, according to the weather, in order to avoid chilling of the body surface Exposure to infections should be strictly avoided. This means the avoidance of crowded movies, or meeting rooms and of attending to any sick person Enough sleep and rest should be had at all times. Proper food is necessary Frequent cardiovascular examinations are called for to determine the cardiac status from time to time

If signs and symptoms of congestive failure develop, the patient should

be put to bed at once. Absolute bed rest is also essential if any infection or infectious disease occurs The length of time bed rest is to be had depends on the severity of the condition The patient is not to leave the bed until all signs and symptoms of failure or of infection subside.

In mild grades of congestive failure, bed rest alone is often sufficient to restore compensation If symptoms and signs continue after one or two days of bed rest, digitalis therapy is called for

In most instances, such medical management carries the patient through the entire period of pregnancy safely Termination of pregnancy should not be considered except in cases belonging to Groups II and III, or if congestive failure occurs in the first two months of pregnancy and it can not be controlled by rest and digitalization. After the fifth month, induction of labor is at least as hard on the patient as normal delivery at term, and pregnancy should, if possible be allowed to continue. The author has observed several very serious cases of decompensation which developed after the fifth month, where continued bed rest, digitalization and general care carried the patient through to full term and normal delivery Smith[17] feels that induction of labor before term is a more serious trial than normal labor at term

Termination of pregnancy in the later months should only be undertaken in those infrequent cases where continuation of pregnancy would definitely endanger the life of the patient and would have an effect of seriously aggravating the existing cardiac disability

The method of delivery to be employed whether from below or by Caesarean section, is to be left to the experienced obstetrician The consensus is that the natural method of delivery from below is best This would appear logical inasmuch as uterine contractions gradually occlude the placental circulation in repeated steps and thus prepare the general circulation for the final occlusion at birth, as discussed in the early part of this chapter This prevents a sudden overburdening of the heart by an abrupt shutting off of the placental circulation as occurs in caesarean delivery

The choice of anesthesia is to be left to an experienced anesthetist. Ether is, perhaps, best when vaginal delivery is done In some cases oxygen may be added Low spinal or caudal anesthesia is to be left to one who has much experience with this method.

The immediate postpartum period is to be carefully watched. Sudden decompensation in a marked degree may occur for reasons described in the early part of this chapter If it occurs, and the venous pressure rises high, a phlebotomy may, at times, be life saving. Of course, bed rest, digitalization and the mercurial diuretics are to be used as in any other cases of decompensation, described in Chapter XIII.

The Effect of Pregnancy on Heart Disease

The question as to whether pregnancy aggravates existing heart disease, thus ultimately shortening the life of the patient, can be answered only by a study of the longevity of a large number of comparative cardiac cases among nulliparous and parous women Comparatively few reports, however, have appeared in the literature in the past, covering such cases

From the few reported series of cases, it appears that pregnancy has no definite aggravating effect on the heart. Thus, Gilchrist and Murray-Lyon[18] studied the longevity of 109 autopsy cases who died as a result of mitral stenosis. Of these, there were 40 males, 28 nulliparous and 41 parous women The average age at death was 39 3 years for males, 42.1 years for nulliparous and 42 0 years for parous women Boyer and Nadas[19] found no difference in the average age at death in rheumatic heart disease in a series of 103 parous women with one or more pregnancies and 49 nulliparous women Furthermore, even multiple pregnancies did not reduce the average age at death There was also no appreciable increase in the size of the heart by repeated pregnancies

On the other hand, in a series of 100 cases with cardiovascular disease followed for two years after confinement, Harris[20] found that 5 died within six weeks of delivery and 5 others within the two year period Four others died from other causes than heart disease Of the remaining 86 cases, 48 were the same as before delivery and 38 showed a definite increase in cardiac disability

Of 202 cardiac cases followed by Bramwell and Longson,[11] 26 died within six months and 10 in more than one year after confinement Of the remaining 166 cases, 135 were still alive after more than one year and 31 after less than one year of the follow-up

It appears that the incidence of death and disability in the last two series is unusually high In the author's personal experience, he found that although an occasional case of cardiac disability and death does occur, which is traceable to the strain of pregnancy and labor, the number is comparatively small In many cases of disability and death, other contributing factors, discussed before, may be the main underlying cause

There is a rare form of acute myocardial degeneration occuring in pregnancy and especially in the puerperium, in women with previously normal hearts, described by Gouley and co-workers[21] It is characterized by an insidious onset of heart failure late in pregnancy which persists during the puerperium At necropsy, disintergration of myocardial fibers with fibroplastic replacement is seen Hypertension may be a factor in some instances It may be mistaken for phlebitis, pelvic infection and subacute bacterial endocarditis

REFERENCES

[1] Dieckmann, W. and Wagner, C : Blood volume and total hemoglobin variations in preg nancy and puerperium Central Society for Clinical Research; Chicago, Nov. 1932 J A M A 100 67, 1933, Arch Int. Med. 53 188, 1934.

[2] Manchester, B , and Loube, S D The velocity of blood flow in normal pregnant women Am Heart J 32:215, 1946

[3] Burwell, C S . The placenta as a modified arteriovenous fistula, considered in relation t the circulatory adjustment to pregnancy. Am J M Sc. 195 1, 1938

[4] Thomson, K J , Reid, D E., and Cohen, M E Studies on circulation in pregnancy Am J M Sc. 198 665, 1939

[5] Widlund, G · The cardio-pulmonic function during pregnancy Upsala, Sweden, Unive sity Clinic of Obstetrics and Gynecology, 1945.

[6] Brown, E , Sampson, J J , Wheeler, E. O , Gundelfinger, B F , and Giansiracusa, J. E Physiologic changes in the circulation during and after obstetric labor Am. Heart J. 3 311, 1947

[7] Sampson, J J , Rose, E M , and Quinn, R.. Estimation of work of obstetric labor and i significance in heart disease Am. J Obst & Gynec 41 36, 1941

[8] Hamilton, B. E Report from the cardiac clinic of the Boston Lying-In Hospital for the fir twenty five years Am Heart J 33 663, 1947

[9] Osman, A A Swelling of the feet and ankles not associated with albuminuria or gross o ganic disease Pathogenesis and treatment of common symptoms Brit. M. J 1 780, 193

[10] Sodeman, W A Cardiac changes in pregnancy unrelated to the usual etiological types heart disease Am. Heart J 19 385, 1940

[11] Sigler, L H · Heart block and pneumonia complicating pregnancy Am. J. Obst. & Gyne 33 157, 1937.

[12] Herrmann, G , and King, E L Cardiovascular disturbances in the obstetric patien J A M A 95 1472, 1930

[13] Quintin, T. J Complete heart block in pregnancy—Report of two successful deliverie Canad M. A. J. 55 600, 1946.

[14] Bramwell, G , and Longson, E A Heart Disease and Pregnancy London, New Yor Toronto, Oxford University Press, 1938.

[15] Carr, F B , and Hamilton, B. E . Five hundred women with serious heart diseases, followe through pregnancy and delivery. Am J. Obst & Gynec. 26 824, 1933

[16] Chesley, L C , and Annitto, J E Pregnancy in the patient with hypertensive diseas Am J Obst. & Gynec. 53 372, 1947

[17] Smith, G B The ante-natal clinic. Brit. M. J. 1 442, 1925.

[18] Gilchrist, A. R , and Murray-Lyon, R M Does pregnancy hasten fatal termination in rhe matic heart disease? Edinburgh M J 40 587, 1933

[19] Boyer, N. H , and Nadas, A S The ultimate effect of pregnancy on rheumatic heart di ease Ann Int Med. 20 99, 1944

[20] Harris, K.: Heart disease with normal rhythm complicating pregnancy, Series of 100 case Lancet 1 677, 1937

[21] Gouley, B. A , McMillan, T M , and Bellet, S . Idiopathic myocardial degeneration ass ciated with pregnancy and especially the puerperium Am J. M. Sc. 194 185, 1937.

CHAPTER XXXI

Surgery and Cardiovascular Disease

STRUCTURAL disease as well as functional abnormality of the cardiovascular system often carries considerable hazard in surgery. Even if we are exceptionally careful in selecting cases for operation, and we employ proper preoperative and postoperative measures, unexpected death may result in some cases

We shall attempt to present here, the forms of cardiovascular disease that may add to the risk of, or may follow a surgical procedure, and discuss the various precautions to be used.

CARDIAC DISEASE AS A SURGICAL RISK

There are comparatively few reports in the literature on the incidence of cardiovascular mortality and morbidity resulting from operation in the presence of cardiac disease, as compared to non-cardiac cases We, therefore, have no definite data for comparison in the two groups The few reported series would tend to indicate that certain forms of well compensated heart disease carry no greater risk than noncardiac cases Thus, in 414 cardiac patients who underwent 494 operations, Butler and co-workers[1] found an over-all mortality of 12 1 per cent, of which 6 3 per cent were unexpected deaths The unexpected mortality rate in 120 cases of well compensated valvular disease was only 2 1 per cent and in 138 cases of "chronic myocarditis," only 4 9 per cent. Sprague,[2] on the other hand, found a postoperative mortality rate of 24 7 per cent in 170 cardiac cases. Two-thirds of the patients were over 50 years of age The marked differences in the mortality rates in these reports may, perhaps, be due to variations in the severity of heart disease and the conditions for which operations were performed In a postoperative study of 336 cardiac cases, Hickman and co-workers[3] found a mortality rate of 2 per cent due to the operation and anesthesia

Certain forms of heart disease carry a distinct risk in surgery, and in some, the risk may be grave This is particularly true in acute coronary thrombosis. Among the 414 cases reported by Butler and co-workers, there were 20 cases of coronary thrombosis, 8 of whom died, with a mortality rate of 44.5 per cent

Cardiac decompensation due to any form of heart disease carries the next serious operative risk, the mortality rate ranging between 15 and 33 per cent The risk corresponds with the degree of decompensation.

Other forms of heart disease that carry serious operative risks are angina

Selection of Cases for Surgery

To decide if surgery may safely be undertaken in a patient suffering from cardiovascular disease, we must consider the urgency of surgery and must have a clear appraisal of the extent of the cardiovascular disease.

Any acute disease which immediately threatens the life of the patient, if unoperated on, such as acute appendicitis, perforation of an abdominal viscus, uncontrollable gastro-intestinal and other hemorrhage, and other emergencies, must of course, be subjected to operation at once, regardless of possible risk A less urgent surgical condition must be considered from various viewpoints. If it will tend to shorten life, or cause great suffering, and particularly if it produces reflex disturbances of the heart or other organs, surgery should be undertaken even if the risk is relatively great For instance, chronic cholecystitis and cholelithiasis with recurring attacks should have surgical interference even if there is considerable risk. Chole cystectomy in most cases will give relief from pain, and may alleviate some of the cardiac and digestive disturbances Prostatic hypertrophy with urinary obstruction should, likewise, be operated on, regardless of how serious the patient's condition may be The author has followed many cases of obstructive prostatic hypertrophy in individuals 60 to 80 years of age and even older with serious heart disease who withstood a two stage prostatectomy and lived several years thereafter in comfort. In some of these cases the cardiac condition has improved after the operation because therapy could be more effectively administered and the patient had more rest and sleep As an example, a patient 84 years old with complete heart block and marked congestive failure developed urinary obstruction due to prostatic hypertrophy. Cardiac therapy was unsuccessful because of extreme restlessness and lack of sleep due to frequent nocturea and pain caused by the obstruction, and also because the diuretics could not be used The surgeon refused to operate because of poor operative risk. The author felt that operation was important because if unoperated on, death would soon ensue as the result of urinary obstruction, uremia and secondary infection caused by catheterization. Furthermore, possible death during operation would, in itself, be relief from suffering He went through a successful two-stage operation and lived in relative comfort for three years, thereafter. The congestive failure markedly dimished by diuretics. He finally died at 87 years of age from a cerebral vascular accident.

On the other hand, operations should not be undertaken in cases where the surgical condition is not serious and does not greatly discomfort the patient. For instance, a uterine prolapse, a cystocele or rectocele, if not severe enough, are best to be left alone if the operative risk, due to cardiovascular disease, is great. The same is true of uncomplicated hernias,

chronically diseased tonsils and, perhaps, nontoxic goiters. Although the condition may become aggravated in later life, we must realize that in severe cardiovascular disease the life expectancy is relatively short. In thyrotoxic states, however, thyroidectomy is advisable even in congestive heart failure, as discussed in Chapter XXVIII

Those conditions that can be successfully treated by x-ray or radium should receive the benefit of such treatment, rather than resort to surgery. For instance, a large uterine fibroid may often be successfully reduced in size by x-ray. This treatment should, therefore, be tried first, before risking surgery.

The Appraisal of Cardiovascular Disease: This must be based, not so much on the amount of structural damage of the heart and blood vessels, but on the degree of incapacity such damage produces. This is determined by the functional capacity of the heart as outlined in Chapter XIII, or by the severity of the anginal syndrome, if present, as discussed in Chapter XIV, or by the extent of local interference with the blood supply to various tissues of the body in the presence of arteriosclerosis or other arterial disease, as discussed in Chapter XIX. Also, an important factor to be considered is the degree of vago-sympathetic sensitivity which the patient presents This may be ascertained from the history of past reactions of the individual to psychic trauma, and to some extent, also, from the degree of hypersensitivity of the carotid sinus reflex

Management of the Cardiovascular Case in Surgery

Although every case submitted to surgery requires careful preoperative, operative and postoperative care, a case presenting cardiovascular disease or disturbances, requires much greater attention. This is true, especially in the arteriosclerotic age

Preoperative Care: Patients presenting auricular fibrillation with or without congestive failure should receive a sufficient amount of digitalis to slow the ventricular rate to within normal limits before operation. If surgery is not urgent, congestive failure with or without auricular fibrillation should be relieved by bed rest, digitalis and the mercurial diuretics before operation is undertaken. Aside from such cardiac therapy, when indicated, preoperative medication should be limited to a minimum. Excessive use of depressants is harmful, especially in individuals over 50 years of age

Reassurance is most essential, especially in emotional individuals and in those who give a history of fainting Cases that present a hyperactive carotid sinus reflex may also have hyperactivity of the vagal system throughout. As a prophylactic measure for possible cardiac standstill,

that may occur in such cases, especially when operation involves the manipulation of highly sensitive vagal areas, Thompson and co-workers[9] suggest the preoperative use of drugs that diminish the vagal effect. Atropin is best for that purpose. They also advise local injection of topical application of procain hydrochloride at the site where the afferent impulses originate, as in the arch of the aorta, hilus of the lung, or other operative areas in thoracic surgery. Inasmuch as morphine is a vagotropic drug, it should be used with great caution, preoperatively, in these individuals If at all necessary, it should be given with atropin. Demerol 50 to 100 milligrams is much safer and may often be as effective.

Operative Care: There is a divergence of opinion as to the best anesthetic in cases with cardiovascular disease To the author's knowledge, no wide study has been made of the relative merit of one anesthetic over the other in any given case and we must rely, therefore, on general impressions. Of greater importance than the anesthetic used is the amount given, and the care with which it is used As Marvin[10] rightly remarked, "It is far more important to select the proper anesthetist than it is to select the proper anesthetic " Most of the fatalities that occur during an operation are due to improper and careless use of anesthesia by men who are not sufficiently trained for this work. Other factors, however, may also be contributory.

In a report on 307 operative fatalities analyzed by the Anesthesia Study Commission of the Philadelphia County Medical Society, Ruth and co-workers[11] observed that in 144 or 47 per cent, death could have been prevented, and in 47 or 15 per cent of the others, it might have been prevented. Only 117 or 38 per cent of the cases were classified as nonpreventable. They list as probable causes of death, overdosage of anesthesia, injudicious selection of anesthetic, inadequate or unindicated therapy, inadequate nursing care, and unindicated intracardiac injection of epinephrine or other drugs instead of rhythmic inflation of the lungs in respiratory paralysis The probable causes of death, named in order, were cardiac failure, respiratory failure, respiratory obstruction, cardiorespiratory failure, asphyxia by vomitus and ventricular fibrillation, the most frequent being cardiac failure

As for the anesthetic used, these authors found that cyclopropane resulted in a large incidence of preventable deaths. The same was true of ether when used by the open drop method The largest number of preventable deaths occurred by the use of tribromethanol and nitrous oxide-oxygen.

Hickman and co-workers[3] believe that inhalation anesthesia, particularly ethylene and oxygen, is safe in cardiac cases, particularly when a high

percentage of oxygen is used. They also found that local anesthesia is good. Spinal anesthesia, as well as ether and nitrous oxide-oxygen, increased the number of postoperative complications and death

Cardiac standstill or ventricular fibrillation occurring during operation, which may happen occasionally even in a structurally normal heart, require energetic treatment by artificial respiration and cardiac massage. Barber and Madden[12] believe that if proper measures are carried out within three minutes, normal cardiac function may be restored. They advocate the transthoracic approach in performing cardiac massage. This is accomplished by opening the chest in the third or fourth interspace, close to the costal cartillages, by a transverse incision, retracting the ribs and massaging the heart with the fingers. Beck[13] advocates the injection of 5 cc. of 2 per cent procain in the right auricle or right ventricle in ventricular fibrillation, and massaging the heart so as to push the drug *through the lungs, and thus into the left chambers, the coronary system* and the myocardium. At the same time, two large metal electrodes are placed on each side of the heart and electric shocks of 1 to $1\frac{1}{2}$ amperes are sent through the myocardium. If no contraction occurs, 1 cc of epinephrin is injected

Thompson and co-workers[9] consider cardiac resuscitation to be really an attempt to restore the cardiorespiratory function, not the cardiac contractions alone. They advise artificial respiration or mouth-to-mouth insufflation, the injection of adrenalin in the right auricle and cardiac massage They stress the importance of injecting the drug in the right auricle, not in the ventricle, for in the latter condition it may produce greater irritability of the myocardium and predispose to ventricular fibrillation

Postoperative Care The most serious complications that may develop during the late stages of prolonged operations and during the postoperative period are shock, heart failure, arterial thrombosis, venous thrombosis with pulmonary embolization and in rare cases, air embolization Any of these conditions may develop even in individuals who previously had no tangible evidence of structural cardiovascular disease. They occur, however, far more frequently in the presence of such disease

Shock is the most frequent complication. A full description of its manifestation has been given in Chapter XVI. It may develop during the operation or in the early postoperative period If it develops suddenly during the period of convalescence, it may indicate the onset of such serious complications as arterial thrombosis, pulmonary embolization from venous thrombosis, hemorrhage or some surgical complication. It is important, therefore, to make a careful search in such cases, for these possible con-

ditions. We must bear in mind the fact that pain in any of these cases may be an unimportant symptom, being either absent or slight. For instance, in postoperative coronary thrombosis, the outstanding finding may be cyanosis and dyspnea in addition to the shock, but very little, if any pain may be present The condition may resemble pulmonary embolization In postoperative evisceration, likewise, pain may be an unimportant complaint.

The treatment of shock consists of copious administration of fluid and the use of oxygen by inhalation. Warm applications to the surface of the body, such as warm blankets and so on should *not* be employed. The opiates or barbiturates may be of value only when there is restlessness. Digitalis is not to be used except when auricular fibrillation or flutter is present with a rapid ventricular rate. The therapy of shock has been discussed more fully in Chapter XVI.

Application of heat to the surface of the body in shock is contrary to the physiologic principles involved. The coldness of the surface of the body is due to universal vasoconstriction of the superficial arterioles and is a protective mechanism to divert the blood to the vital organs of the body, particularly the central nervous system, as was discussed in Chapter XVI It is, therefore, irrational to apply warmth to the surface of the body which would divert the blood to the skin and thus deprive the vital organs of whatever blood supply they may get. Blalock[14] stresses the detrimental effect of heat application in shock.

Heart failure occurring postoperatively is to be treated the same as under other circumstances, as discussed in Chapter XIII. We must always be sure, however, not to mistake shock for heart failure The author has seen a number of cases suffering from shock who were treated for heart failure because of rapid heart rate, and the presence of some pyspnea and pulmonary rales The importance of clearly differentiating the two conditions lies in the fact that shock requires massive administration of saline solution, while in heart failure such administration may be detrimental.

Postoperative arterial and venous thrombosis are serious complications which may often prove fatal Their frequency of occurrence has been greatly reduced in recent years by the use of anti-coagulants, discussed in Chapter XIX, and by allowing the patient out of bed as early as possible

In cases where the operation is prolonged, especially if the operative field is in the pelvis, and where there is evidence of venous thrombosis or varicosities, 300 milligrams of heparin may be given the first day after operation together with 200 to 300 milligrams of dicumarol. This is to be followed by similar subsequent daily doses of dicumarol, controlled by a daily prothrombin time determination as described in Chapter XIX.

The dicumarol may be continued as long as there is danger of possible thrombosis.

Allowing the patient out of bed one or two days after operation has been found to have a definite beneficial effect on the circulation and to help prevent arterial and especially venous thrombosis.

REFERENCES

[1] Butler, S. Feeney, N., and Levine, S A. The patient with heart disease as a surgical risk. J A.M.A. 95 85, 1930.

[2] Sprague, H B · Heart in surgery Surg Gynec & Obst 49 54, 1929

[3] Hickman, J, Livingstone, H, and Davies, M E: Surgical and anesthetic risks in cardiac disease Arch Surg 31·917, 1935

[4] Schnedorf, J G, Lorhan, P. H, and Orr, T G Problem of anoxia in surgery and anesthesia. Arch Surg. 43:169, 1941.

[5] Blackford, J M, and Willius, F A · Operative risk in cardiac disease. J A M.A 69·2011, 1917.

[6] Currens, J H, White, P D, and Churchill, E D Cardiac arrhythmias following thoracic surgery. New England J Med 229.360, 1943

[7] Bailey, C C. and Betts, R. H Cardiac arrhythmias following pneumonectomy New England J Med 229·356, 1943

[8] Turner, F. P., and Wilkenson, F A. H Operating room deaths Study of 23 consecutive cases in which autopsies were performed Am J Surg 57 242, 1942

[9] Thompson, S A, Birnbaum, G L, and Shiner, I S Cardiac resuscitaton J.A M A 119 1479, 1942.

[10] Marvin, H M: The heart during anesthesia and operative procedures. New England J. M. 199·547, 1928.

[11] Ruth, H S, Hangen, F. P, and Grove, D D Anesthesia study commission· Findings of 11 years activity J.A.M.A 135 881, 1947

[12] Barber, R. F, and Madden, J L · Resuscitation of heart Am J Surg 64 149, 1944

[13] Beck, C. S Resuscitation of cardiac standstill and ventricular fibrillation occurring during operation Am J Surg 54 273, 1941

[14] Blalock, A. A comparison of the effects of the local application of heat and of cold in the prevention and treatment of experimental shock Surgery 2·356, 1942

Index